VOL. 36 MAY 1960 NO. 5

BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

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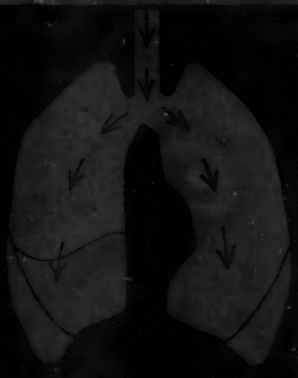

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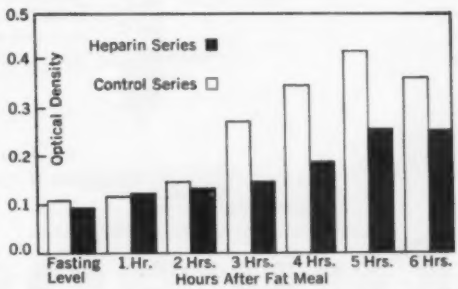
1. Fuller, H. L.: Angiology 9:311 (Oct.) 1958.
2. Shaftel, H. E., and Selman, D.: Angiology *10*:131 (June) 1959.



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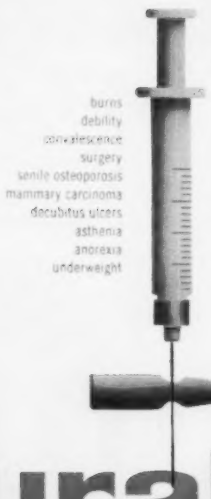

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*Miller, J.B., et al.: Ann. Allergy, 12:611, Sept.-Oct., 1954.

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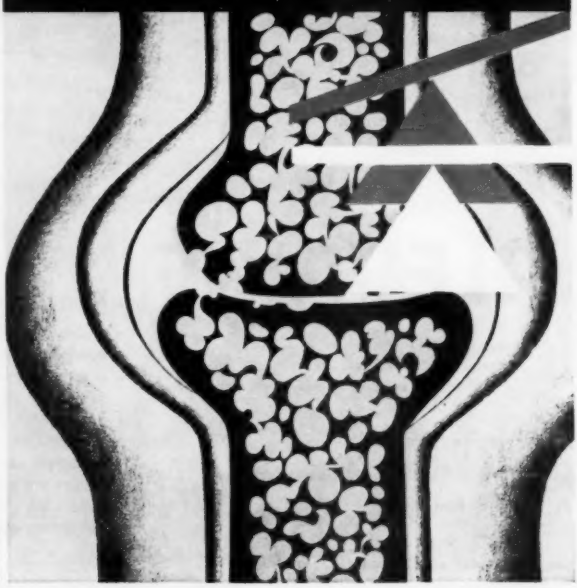

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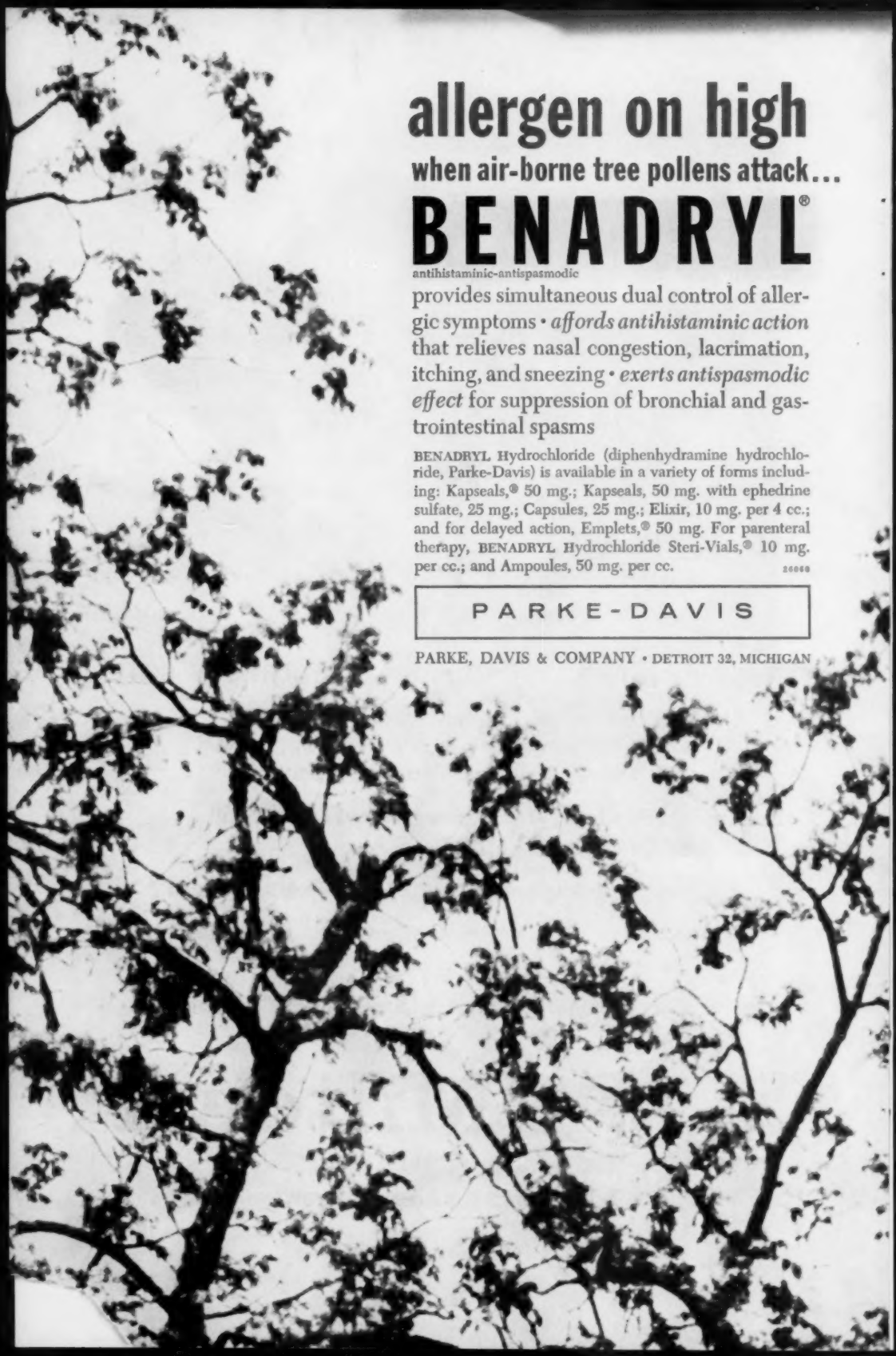

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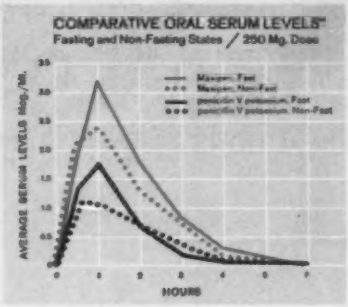

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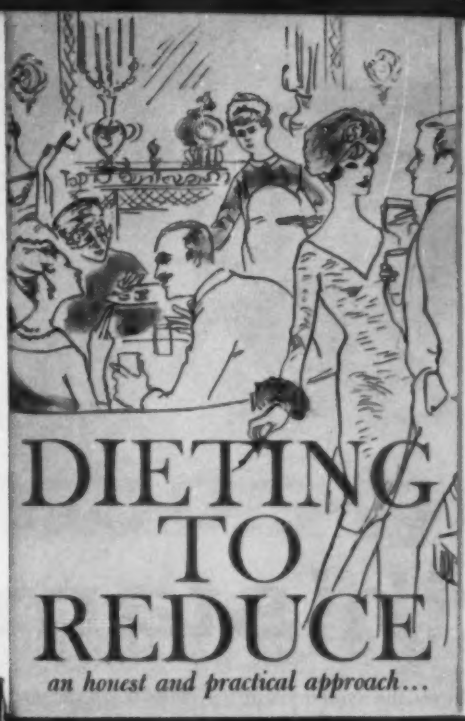

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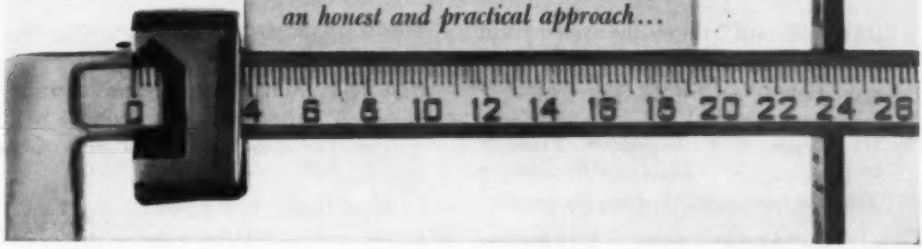

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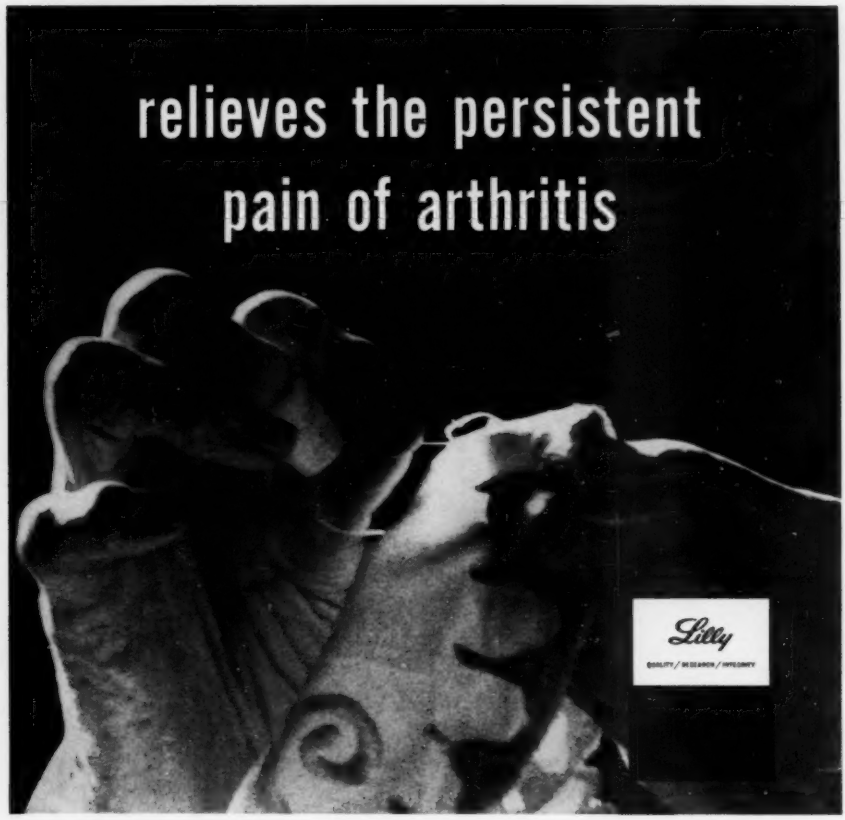

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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

ROBERT L. CRAIG, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
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VOL. 36, NO. 5 MAY 1960

JACKSON AND FREUD: THE RELATION OF DISSOLUTION TO REGRESSION*

LOUIS LINN

Associate Attending Psychiatrist, The Mount Sinai Hospital, New York, N. Y.

IN 1891 Freud described aphasia as a retrogression or dissolution of the speech apparatus to an earlier mode of function under pathologic conditions. This point of view, based on the work of Hughlings Jackson, took issue with the localization theories then popular. It is to Freud's contact with Jackson at this point that one can trace many of the basic ideas of psychoanalysis. Ideas here expressed concerning the "speech apparatus" were the forerunners of similar ideas in relation to the "psychic apparatus".

While Freud's debt to Hughlings Jackson has long been acknowledged in psychoanalytic literature[1-4], neurologists have somehow overlooked the impact of Jackson's concept of evolution and dissolution of the nervous system on psychoanalytic theory. May I briefly summarize those ideas of Jackson which, it seems to me, have become part of psychoanalysis, and show how the latter, in turn, could be of value to clinical neurology.

Jackson's primary thesis is that the functioning central nervous

* Presented at The New York Academy of Medicine before the combined meeting of the Section on Neurology and Psychiatry and the New York Neurological Society, April 14, 1959.

system of the adult is the end result of an evolutionary or developmental process. The patterns of function and behavior dominant in the first stages of development come under the controlling influence of new patterns as the nervous system matures. These in turn become dominated by others which represent a still more advanced level of organization. The progression involves a transfer of influence from centers which are anatomically complete and comparatively well-organized at birth to others which in the adult state are still evolving. It also involves a transition from automatic behavior patterns to others which are under voluntary control[5]. The highest and most recently acquired functional patterns are also the most vulnerable to trauma. When the central nervous system is subjected to stress, the highest levels are most readily impaired. A direct consequence of impairment is that previously submerged patterns again dominate the clinical picture. For this reversal of the developmental process Jackson borrowed Spencer's term *dissolution*.

Freud's account of the development of the psychic apparatus parallels the schema of Jackson. The period of infancy and early childhood is characterized by relatively simple and stereotyped patterns of behavior. The latter, including the wishes and needs which motivate them, are associated with instinctual biological drives. In time these give way to other learned patterns which are socially more complex. The capacity to contact reality improves. The pleasure-seeking point of view which characterizes the first stages gives way to a more adult appreciation of the demands of reality. The thought processes responsible for this more realistic point of view which exert a controlling and regulating influence on the individual were referred to collectively by Freud as the *ego* and the *super ego*. The infantile impulses brought under their control Freud called the *id*.

The automaticity of the earliest behavior patterns in Jackson's scheme could be compared to Freud's emphasis on the stereotypy of the infantile reactions and to his concept of the system *Unconscious* to which these basic drives are subsequently relegated. The predominance, at maturity, of voluntary behavior which Jackson emphasizes, is reflected in Freud's emphasis on the predominant role of the system *Conscious*, with its associated capacity for more flexibly adaptive behavior in the emotionally mature adult. Under certain conditions of stress, the controlling influence of the ego and the superego becomes

impaired. The balance of power is upset and previously controlled infantile behavior patterns again dominate the clinical picture. To this reversal of the developmental process Freud applied the term *regression.*

Jackson always made the point that dissolution is not necessarily a manifestation of disease. On the contrary, the state of health is characterized by "a rhythm of evolution and dissolution"[6]. This rhythm is encountered regularly in sleep, in dreams and in reveries. Freud made exactly the same point about regression. "Find out about dreams," said Jackson, "and you will find out about insanity." "Dreams," echoed Freud, "contain the psychology of the neuroses in a nutshell" [2]. Jackson often defined the severity of psychopathology in terms of sleep, regarding psychotic reactions analogous to light dreaming sleep as the least severe; those analagous to deeper sleep with somnambulism as the next grade in severity; and those analagous to deep dreamless sleep as the most severe. Recent psychoanalytic theory attempts a similar classification in psychoanalytic terms[7, 8].

Next in importance to Jackson's concept of dissolution is his interpretation of symptoms in terms of negative and positive states. He insisted that a destroyed and therefore absent structure cannot of itself explain symptoms. It can only permit other intact and functioning structures to come to the surface, structures whose manifestations conceivably had been held in abeyance as long as the higher level controlling centers still functioned. He makes the comparison to an overthrown government. The destruction of the governing body makes it possible for anarchic upheavals to occur. These and the gradual return to a new order are manifestations of the groups and individuals who still remain, not of those who are destroyed. This concept is well illustrated by the following penetrating remarks of Jackson about a delirious patient[9]: "Besides his (the patient's) *not knowings* there are his *wrong knowings.* He imagines himself to be at home or at work, and acts, as far as practicable, as if he were. Ceasing to recognize his nurse as a nurse he takes her to be his wife. His delirium is the (expression of) the *survival of the fittest states* on his then highest evolutionary level. Plainly he is reduced to a more automatic condition. Being, negatively, lost to his present *real* surroundings, from loss of function of the highest and latest developed and least organized nervous arrangements, he, positively, talks and acts as if adjusted to some former *ideal* surroundings."

In these extraordinary comments Jackson provides many ideas which are incorporated into the very foundations of psychoanalytic psychology. First of all, he recognizes here the adaptational significance of the patient's behavior. Unable to adapt (or adjust, as Jackson puts it) to the realities of his illness and his hospital surroundings, he wishfully transforms his environment. In his delusional state the hospital is no longer strange and bewildering. In fact it is no longer the hospital but his own home. The nurse who attends him is no longer an impersonal stranger but is his own wife. In a negative sense he retreats from an unbearable reality. In a positive sense he tries to reestablish contact with reality by means of delusional transformations of his surroundings. The delusions are based on the memories of happier experiences in relation to some former ideal. Here is the model for the psychoanalytic concept of psychosis[10]. No psychoanalyst would take issue with Jackson's contention[11] that the clinical picture in psychosis is the result of the complex interaction of four factors: the depth of dissolution (or severity of regression), the patient's premorbid personality, the specific environment to which he is reacting, and the speed with which the dissolution takes place.

Both Jackson and Freud puzzled over the relationship between the psychological and the physiological. Jackson stated[12]: "In all our studies of diseases of the nervous system we must be on our guard against the fallacy that what are physical states in lower centers fine away *into* psychical states in higher centers; that, for example, vibrations of sensory nerves *become* sensations, or that somehow or other an idea produces a movement." Freud made this point of view his own. With Jackson, he regarded the psychological as a dependent concomitant of the physiological[1, 13]. Both acknowledged that the bridge between matter and mind was for them an unapproachable mystery. Jackson toiled largely on one side, the matter side, of this bridge; Freud, on the side of the mind. Yet, though the paths they travelled ran parallel, they often met in non-Euclidean fashion. The following brief examples, selected from a larger group, will show how these points of view are not only parallel but mutually reinforcing.

The Bender Face-Hand Test[14]: The reappearance in the brain-injured adult of a pattern of response to double simultaneous cutaneous stimulation (DSS) which is present normally in childhood is a striking example of the Jacksonian concept of dissolution. The unexpected

dominance of the genital region of a three year old child of either sex on DSS is a striking confirmation from a completely independent line of investigation of basic psychoanalytic theory as to the existence at this early age of the so-called phallic stage. Thus, neurologic and psychoanalytic data seem to concur in the idea that the genital organ is an important locus of the self-concept at this early age. The curious position of the hand as the least dominant element in double simultaneous cutaneous stimulation also lends itself to logical explanation in psychoanalytic terms[15]. Suffice it to say that on the basis of a psychoanalytic approach the positive face-hand test in the brain-injured adult could be regarded as the sensory counterpart of instinctual grasping and sucking.

"Pushing" in Cattle[16]: Certain domestic animals (ungulates) with brain disease push their heads repeatedly and persistently against any vertical surface in their field of vision. In so doing the animals tend to slide the head along the vertical surface until it comes to rest in a corner, where it will stand indefinitely with its head pressed snugly against the two walls as they meet in the corner. This puzzling and apparently meaningless behavior becomes recognizable as one studies the behavior of the newborn animal in its search for the mother's breast. Thus the phenomenon of "pushing" in the ungulate appears theoretically to be a counterpart of instinctual sucking and grasping in humans. These patterns tend to re-emerge not only in relation to brain disease but also as a response to fear or anxiety. Thus, dissolution in response to brain trauma parallels regression in response to emotional trauma.

The Sense of Smell: Elsberg[17, 18] and his co-workers demonstrated that the sense of smell is more acute in normal children than it is in normal adults. One can anticipate this finding on the theory that the four-footed position makes olfaction a more important sensory avenue for contacting the environment, and that with the assumption of the upright position olfaction is surpassed by other sensory receptors. The youngster who is closer to the crawling phase of his development would be expected on the basis of this evolutionary theory to have more sensitive olfaction than the adult. One would predict on the basis of the principles of dissolution and regression that adult patients with clouding of the sensorium would have hyperosmia when contrasted to normal adults. This was indeed Elsberg's finding. It caused him to speculate that in some instances at least increased intracranial pressure was rendering the olfactory nerve hyper-irritable. The dissolution-

regression approach to the problem provides a more reasonable explanation.

Fright Reactions After Electroconvulsive Therapy (ECT): Some patients, on waking up from ECT, react to the first face that they see with great terror. The thought occurred to me that the reaction of these patients was reminiscent of the terrified response of infants around the age of eight months when they are confronted with a strange face. Spitz[19], who studied this phenomenon in detail, made the point that prior to this age infants do not usually distinguish between one face and another. A mother substitute is as acceptable as the mother. However, starting at eight months of age, the infant makes a sharp and vociferous distinction. The sudden appearance of a stranger's face, however friendly, tends to elicit a reaction of terror. Spitz found that he could approach these children walking backwards without eliciting fright; that is, the back of the head of a stranger was regarded benignly; only the face had a traumatic effect. For example, he found that he could back right up to these children and engage their friendly interest by wiggling his fingers at them. Once the child was actively playing with his fingers he could turn around slowly without precipitating the terror reaction. Hypothesizing that the post-ECT patients had undergone dissolution and regression to this "eight-month" reaction pattern, I sat with my back to patients who had previously awakened with terror. After a time the patient would awaken, scrutinize the back of my head with calm interest and inquire quietly who I was. At this point I would move my fingers playfully. The patient would take hold of my fingers and repeat the question. In a friendly voice I would greet him and slowly turn around. Like the eight-month old child, the post-ECT patient would now accept me without terror. This fact was confirmed repeatedly in several cases. An interesting additional practical application of this phenomenon has been described by clinical psychologists who do testing of children. A child who is too frightened to make test drawings while the examiner is facing him will perform quite readily when the examiner turns his back.

Voluntary Eye Movements: A final example concerns itself with the capacity to follow, on command, the movements of an object in the field of vision. It has been observed that the nursing infant will selectively follow the movements of the mother's face at a time when it will disregard other moving objects with which one tries to engage

its attention. Spitz[20] found that the child will also follow a balloon on which a face is drawn, or even a piece of paper on which there is a crude representation of a full face. An identical selective attraction to the moving human face can be demonstrated on neuro-ophthalmologic examination of the adult patient with clouded sensorium due to organic brain disease[21]. Thus, certain brain-injured patients who will disregard the request to follow the moving finger of the examiner will follow the movements of his face or that of a simple graphic representation of the face if instructed to do so.

The presence of the Babinski sign and tonic neck reflexes at birth, their disappearance with growth, and their reappearance in later years in disease, are familiar examples of dissolution. Instinctual sucking and grasping in the brain-injured adult seems to involve psychological regression as well as dissolution. Recently the suggestion was made that certain "psychosomatic" disorders involve dissolution in the reaction patterns of the autonomic nervous system as well as psychological regression[22]. It may be anticipated that research based on the combined principles of dissolution and regression will provide fruitful leads elsewhere.

Conclusion: Dissolution of the central nervous system as measured in neurological terms and regression as measured psychologically tend to parallel each other. The normal developmental process in all its aspects sheds light on the behavior of the adult in health and disease. The work of Hughlings Jackson and that of Sigmund Freud fairly represent two aspects of a common point of view. While the foregoing simple examples, culled from personal experience, are not altogether conclusive, they do, I think, illustrate a basic principle.

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Symposium on*

THE PREVENTION OF OBESITY

Sponsored by the American Heart Association

Presiding: HERBERT POLLACK, M.D.
Chairman, Nutrition Committee, American Heart Association

Part I.

1. AN ANTHROPOLOGICAL APPROACH TO THE PROBLEM OF OBESITY

HORTENSE POWDERMAKER, Ph.D.
Professor of Anthropology, Queens College, Flushing, New York

2. INFLUENCE OF OBESITY ON MORBIDITY AND MORTALITY

HERBERT H. MARKS
Assistant Statistician, Metropolitan Life Insurance Company, New York, N. Y.

3. THE PATHOLOGY OF OBESITY

W. STANLEY HARTROFT, M.D., Ph.D.
Professor and Chairman, Department of Pathology, Washington University School of Medicine, St. Louis, Mo.

4. GENETIC FACTORS IN OBESITY

JEAN MAYER, Ph.D., D.Sc.
Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts

(Part II of this Symposium will be published in the June 1960 issue of the Bulletin)

* Held at The New York Academy of Medicine, May 26, 1959.

AN ANTHROPOLOGICAL APPROACH TO THE PROBLEM OF OBESITY*

HORTENSE POWDERMAKER, Ph.D.

Professor of Anthropology, Queens College, Flushing, New York

I AM THE only person participating in the Symposium who has never done any research on the problem of obesity, and who is decidedly not an expert on the subject. My role here as an anthropologist is to attempt to set the problem in the context of the culture. In this day of specialists we cultural anthropologists are the specialists in a holistic approach. In our studies of primitive or preliterate tribal societies, we have asked questions concerning relationships between different elements of culture. How are the functioning of the family, the economic and class organization, the political system, the religious and magical beliefs, the values that men live by, related to each other and integrated in that abstraction we call culture? In this paper I shall give a cultural approach to the problem of obesity, raise questions, and, quite tentatively, offer some hypotheses. These will provide some understanding of the complexities of the problem and a basis for future research.

In setting the problem of obesity in the frame of the culture of contemporary society, my focus will be on the roles of food and of physical activity in our value systems. Incidentally, I wonder why so much of the education designed to reduce the incidence of obesity is centered on food rather than on activity. Is it assumed that food habits may be modified more easily than those of physical activity?

My basic questions are concerned with the symbolism of fatness and thinness in our society and the relationship of each to other symbols and to our values. I would be interested in differences in the symbols and in the relative strength of the same symbols in class, ethnic, religious, sex, and age groups, and among individuals. I would assume that there might be conflicting values concerning fatness and thinness, about eating and physical activity, as there are in many other areas of our life, and that some of this conflict might stem from the fact that we live in

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a rapidly changing society, where traditional values linger beside new ones. I would also be interested in the cultural study of people who are not obese as well as those who are, i.e., some kind of control group in which variables are limited. As an anthropologist, I am naturally interested in a comparative approach, i.e., the symbolism of obesity and thinness in other cultures and the many-sided role of food and eating in them, assuming that this comparative knowledge would illuminate the problem in our society.

Beginning with the last point, let me summarize briefly some relevant facts from pre-literate, tribal societies. In a large number of these societies the economy was a subsistence one, whether characterized by food gathering, hunting, fishing, agriculture, raising cattle, or some combination of these activities. A major part of all activity was concerned with the production of food. Tools were crude—a wooden hoe and a stone axe. The only means of transportation was by foot or canoe. Food-growing plots were often several miles from the village; the clearing of the dense bush in tropical and semi-tropical parts of the world by the men was a strenuous job, as was also the planting and weeding by the women. Strenuous physical activity was the norm for men and for women, whatever the type of economy. But although everyone worked hard and long in the production of food, hunger was a common experience. Famines and periods of scarcity were not unusual. Seasonal changes, plagues, pests, and many other natural causes tended to produce alternate periods of shortage and relative plenty. It is, therefore, not difficult to understand that gluttony, one of the original sins in our society, was an accepted and valued practice for these tribal peoples whenever it was possible. In anticipating a feast a Trobriand Islander in the Southwest Pacific says, "We shall be glad, we shall eat until we vomit" [1]. A South African tribal expression is, "We shall eat until our bellies swell out and we can no longer stand"[2].

The function of food and eating was, and still is, not restricted to the biological aspects. Food is the center of a complex value system and an elaborate ideology centers about it. Religious beliefs, rituals, prestige systems, etiquette, social organization, and group unity are related to food. Throughout the Pacific, in Africa, and in most other parts of the tribal world, kinship groups work together in the production of food. Distribution of food is part of traditional obligations between people related biologically and through marriage ties, between clans,

and between chiefs and their subjects. The accumulation of food, particularly for ritual occasions, is a major way of obtaining prestige. At all significant events in the individual's life history—birth, puberty, marriage, death—there must be a feast, and the amount of food reflects the prestige of those giving it. Less formal but of equal significance, is the relationship of food-giving to hospitality, valued even more among tribal peoples than among ourselves.

The importance of food is not limited to relations among the living. It plays a significant role in relationships with dead ancestors and gods. Offerings of food are made to them, so that they will grant the requests of the living and protect them from sickness and other misfortunes. The spirits of the dead and the ancestral gods presumably have to eat and, among some tribes, observe the same eating etiquette as do the living. In Haiti the gods are very demanding, and providing their food becomes a means of controlling and manipulating them, for the gods depend on men for their strength. In the same country death is symbolized in many instances as being "eaten" by evil gods and, in a modern context of a railroad accident, the locomotive is said to be a machine that eats people. This oral aggression of evil gods (and, presumably, the locomotive, too) is regarded as being motivated by the desire to acquire strength through being fed[3]. The function of food in magical and religious practices throughout the world is well known, and food taboos are part of many religious rituals in both tribal and modern societies. We could go on almost indefinitely describing the social role of food[4, 5].

But we turn now to the more personal role of food for the individual. The infant's first relationship with his mother is a nutritive one. In primitive societies it is fairly common for a child to be nursed at his mother's breast for several years. For the infant in all societies, suckling and eating appear to be among the earliest sensory experiences and pleasures. The psychoanalysts call it the oral stage. We tend to agree with them that early infantile experiences have lasting effects. In some tribal societies such as the one I studied in the Southwest Pacific, the stomach is the seat of the emotions. "Bel belong me hot" is the pidgin English way of expressing deep feeling, whether occasioned by anger, sexual desire, or eating well[6]. The same concept appears in Africa and other parts of the world.

Given the scarcity of food and the ever-present fear of famine in

many tribal societies, the significant social role of food, and the lasting impact of the infant's first sensory satisfactions, it is not surprising to find that stoutness or some degree of obesity is often regarded with favor. This is particularly true for the concept of female attractiveness. Among the Banyankole, a pastoral people in East Africa, when a girl began to prepare for marriage at the age of eight, she was not permitted to play and run about, but kept in the house and made to drink large quantities of milk daily so that she would grow fat. By the end of a year she could only waddle. "The fatter she grew the more beautiful she was considered and her condition was a marked contrast to that of the men, who were athletic and well-developed." The royal women, the king's mother and his wives, vied with each other as to who should be the stoutest. They took no exercise, but were carried in litters when going from place to place[7].

Among the Bushmen of South Africa, the new moon is spoken of as a man because of its slenderness, and the full moon is a woman because of its roundness. Masculine and feminine endings are given to the same roots to denote sex: male endings for strong, tall, slender things and female for weak, small, round ones[8]. Today in a mining community on the Copperbelt of Northern Rhodesia where I have done fieldwork, in one popular song a young man sings,

> "Hullo, Mama,* the beautiful one, let us go to town;
> You will be very fat, you girl, if you stay with me".

The standard of beauty for a woman here was not the fatness which we mentioned earlier, but rather a moderate plumpness.

Summarizing briefly for tribal pre-literate societies, we note that hunger was common and that a high proportion of men's and women's energy was spent in producing enough food to stay alive; that food was not only a biological necessity, but that its social and psychological functions were also very significant. The giving of food was a prominent part of all relationships: between kindred, between clans, with dead ancestors, and with gods. Food played a role in ritual, magic and witchcraft, and in hospitality. The accumulation of food was a mark of great prestige. Fatness was a mark of beauty and desirability in women.

We turn now to our contemporary society. It is characterized by an economy of plenty as compared to the economy of scarcity in tribal societies. We eat too much. We have too much of many things. Ac-

* "Mama" is a term of address for a woman.

cording to the population experts, there are too many people in the world, due to the decline in mortality rates. A key theme in this age of plenty—people, food, things—is consumption. We are urged to buy more and more things and new things: food, cars, refrigerators, television sets, clothes, etcetera. We are constantly advised that prosperity can be maintained only by ever-increasing consumption. This is in sharp contrast to our own not too distant past, when saving and thrift were among the prized virtues and emphasis was on production rather than consumption.

Another important change in our modern industrial society is that physical activity is almost non-existent in most occupations, particularly those in the middle and upper classes. We think of the ever-increasing white-collar jobs, the managerial and professional groups, and even the unskilled and skilled laborers in machine and factory production. For some people there are active games in leisure time, probably more for males than females. But, in general, leisure time activities tend to become increasingly passive. We travel in automobiles, we sit in movies, we stay at home and watch television. Most people live too far away to walk to their place of work. Walking for pleasure is very rare. Former President Truman's daily walk is regarded as one of his peculiarities. The trend for those who are advised to take exercise and who also have the necessary wealth is a passive form—massage, the electric table which vibrates the body, and other electrical devices.

But while people may exercise less and live in an economy of plenty, they are becoming increasingly aware of the problem of obesity. There is a continuing enlargement of our knowledge of nutrition, of the relationship between obesity and certain diseases, and to health and longevity in general, and a wide popularization of this knowledge. This past month we had a "Nutrition Week", and every day our mass media—newspapers, radio and television—carry information about food and its relationship to health, disease and physical attractiveness.

Our standards of beauty, particularly for the female, have undergone a great change from tribal societies and from our own past. The slender, youthful-looking figure is now desired by women of all ages. The term "matronly", with its connotation of plumpness, is decidedly not flattering. Although the female body is predisposed to proportionately more fat and the male to more muscle[9], the plump or stout woman's body is considered neither beautiful nor

sexually attractive. Our guess is that a hundred years ago the term "matronly" was not unflattering. The role of a wife today as an active sex mate, as compared to her role in our more Puritanical past with its emphasis on motherhood rather than on the pleasures of sexual experiences, may be significant in this context. For this and for other reasons the contemporary cult of youthfulness appears to be stronger among women than among men. At almost any middle and upper class gathering of middle-aged men and women, a large proportion of the latter will have dyed their hair, while most of the men will have the symbolic grey hair of aging. It is generally assumed that physical attractiveness is more important for the female than for the male in their respective search for a mate. Success, wealth, and vigor are significant eligibility criteria for potential husbands and fathers. Of course, sex appeal is important for men, too, but it seems not to be so much associated with seeming youthfulness as it is for women.

However, the cult of youthfulness is not confined to women. As science enables us all to live longer and longer, men and women want to remain young longer and longer. This is not a new desire. The quest for the fountain of youth is one of the well-known themes in mythology. The desire to remain healthy and "fit" as long as possible seems quite normal to us. Yet our excessive need to *look* young may also be related to other trends in our culture. Middle-aged people often find it difficult to get jobs, and they are faced with enforced, and sometimes unwanted, retirement at a fixed age. The cult of youthfulness may also have some connection with our apparent concern about sexual potency and sexual pleasure. Many books and articles discuss these as a difficult problem, and their large sale presumably indicates considerable anxiety about sexuality in our culture. Do people with this kind of anxiety have more, or less, difficulty in dieting and keeping their bodies young-looking?

We have indicated a number of strong trends in our culture which run counter to obesity. The desire for health, for longevity, for youthfulness, for sexual attractiveness is indeed a powerful motivation. Yet obesity is a problem. Otherwise, we would not be participating in this Symposium. We ask, then, what cultural and psychological factors might be counteracting the effective work of nutritionists, physicians, beauty specialists, and advertisements in the mass media? We have a number of hypotheses. We think there may be considerable ambivalence for many people in regard to being fat or thin, to over-eating or

to dieting. This ambivalence could, in turn, come from conflicting patterns in our culture.

I have a hypothesis that, consciously or unconsciously, our symbolism for a maternal woman is on the plump or obese side. There is the figure of a pregnant woman and, as already indicated, the infantile satisfactions gained from food given by a mother or mother-surrogate. The image for mother and for mate may be in conflict.

Then, too, food is a very significant symbol in our prestige system. The kind of food, the quantity, and the manner in which it is served are among the important criteria of social class. In most tribal societies, even those with a highly stratified social system, everyone—royalty and commoners—ate the same kind of food, and if there was famine everyone was hungry. In our society there are sharp distinctions. Although there are probably relatively few people today who know sustained hunger because of poverty, poor people eat differently from rich people. Fattening, starchy foods are common among the former, and in certain ethnic groups, particularly those from southern Europe, women tend to be fat. Obesity for women is therefore somewhat symbolic for lower class. In our socially mobile society this is a powerful deterrent. The symbolism of obesity in men has been different. The image of a successful middle-aged man in the middle and upper classes has been with a "pouch", or "bay-window", as it was called a generation ago. We are all familiar with pictures of this type, resplendent with gold watch chain across the large stomach. Today this particular male class-symbolism is changing, probably because of the increased knowledge of the relationship of obesity to heart-malfunctioning and to other diseases.

Although slenderness becomes increasingly a symbol of social status, the food of the wealthy is still rich and plentiful, and their dinner parties are often, quite literally, a sign of conspicuous consumption. With the ever-increasing diversity of foods, food has become not only a matter of social status, but also a mark of one's personality and taste. More and more people are becoming gourmets, and with the declining number of servants, the hostess—and often the host, too—display their individual style and taste in cooking[10]. We become more personally interested in food as we become more aware of the problems connected with overeating.

The giving of food to people who are in trouble is a still widely prevailing folk custom and is reflected in our radio "soap operas". When

someone is having marital or financial problems, or when there is illness in the family, a good neighbor brings in food and says, "You must eat to keep up your strength". The same correlation of eating with strength runs through many food advertisements, particularly those designed to reach young, growing children in the television audience. It would be interesting to do an analysis of the mass media advertisements of food which are directed toward children. It would be equally desirable to analyze the advertisements concerning reducing foods, pills, and other products, directed toward adults.

Our symbols for fatness or thinness are not clear-cut, as old and new patterns mingle. We have the beliefs that fat people are good-natured, contented, likable, funny, and also that they are foolish, "greasy", and greedy. There is the well-known image from Shakespeare's *Julius Caesar*, in which Caesar prefers his followers to be fat, and fears those who are lean and hungry*. A study of heroes and heroines and villains in our mass media, in terms of their fatness and thinness, might be revealing. I cannot offhand remember any fat movie villains, male or female. But this would be interesting to check.

While the family in our society is no longer an economic unit for the production of food, as it was in primitive society, the family meal remains one of the few times when the family is united and drawn together. Parents still are the givers of food, and most of us are aware of the intense interest with which young siblings watch mother cut a pie and their anxiety over whether the slices are even. This is true in homes where food is plentiful, and obviously food is a symbol for the mother's favoring or not favoring one child more than another.

Eating well, a full stomach, is still one of our main ways of achieving a state of euphoria. A really good dinner sets all of us up. This is probably connected with the fact that one of the earliest forms of security and of sensory pleasure is connected with the intake of food, and that about it are centered the first human relations. The eating of food and the giving of it thus remains a symbol of love, affection, and friendliness, as well as a source of pleasure in itself.

It is often stated and rather commonly believed that indulgence in overeating is a conscious or unconscious compensation for frustration

* "Let me have men about me that are fat,
Sleek-headed men, and such as sleep o'nights:
Yond Cassius has a lean and hungry look;
He thinks too much: such men are dangerous."
Shakespeare, William, *Julius Caesar*, Act I, Scene 2.

or neurotic problems. We ask a further question: why do some people seek this form of compensation rather than another form? Is there, for instance, one type of person who tends to be alcoholic and another to overeat? A number of studies have indicated a comparatively low rate of alcoholism among Jews[11, 12]. They show that sobriety is a strong moral virtue among orthodox and pious Jews, and that drunkenness is associated with the outgroup, the Gentiles. The Jewish norms of moderate drinking and sobriety are bound up with the ceremonial and ritual observances, with their religious beliefs, and with the value of remaining separate from Christians. It is assumed that Jews have the same proportion of neurotic and other problems that could lead to alcoholism as do Christians. The norms favored by any group for meeting problems are part of its culture and are internalized in childhood. It would be interesting to find out whether overeating and obesity are more common among orthodox Jews than among reformed Jews and Christians of the same class. We think, too, that there could be regional as well as religious differences in attitudes toward obesity. One suspects that there would be considerable difference between the South and New England.

We have a number of other questions concerning possible correlations of cultural and psychological factors with obesity. Is the ability to diet, and to diet consistently, related to belief in a measure of control over one's fate? Is it related to the strength of the belief in science? Is obesity correlated with orientations toward asceticism versus sensory pleasures? Has there been any study of obesity among monks and nuns? Do people who value sensory pleasures in general, such as those derived from perfumes, from physical contacts, from sexual experience, demonstrate an ability to diet more, or less, successfully than others? The degree of emphasis on sensory pleasure may be culturally determined, may vary from one historical period to another in the same culture, and from one class and ethnic group. And within each group there can be variations due to genetic idiosyncratic factors in the life history of individuals.

There are time limits to the number of questions we can raise. We have tried to indicate some of the cultural factors underlying the problem of obesity. Our society, with its economy of plenty and lack of physical activity, as compared to the economy of scarcity and the hard physical work in tribal societies, provides increasing opportunities

for people to eat more food and to become obese. At the same time, other cultural factors, such as the knowledge of nutrition and of the relationship of obesity to disease and longevity and the popularization of the knowledge, our cult of youthfulness and the emphasis on the beauty of the slender body, particularly for the female, our class stereotypes, all tend to keep people from taking advantage of the opportunities to gorge on food. Yet there are many who overeat. We have hypotheses that this may be related to our deeply imbedded desire for the euphoria which comes from a full stomach, with other sensory indulgences or a lack of them, with conflicting imagery about a motherly woman versus a sex mate, with the use of food as a status symbol and as an expression of personality tastes, and with cultural norms about food and standards of beauty in different religious, class, ethnic, and regional groups. We have asked a number of questions relating to possible cultural correlations, for which there is no data. Mainly we have tried to show some of the intricate and complex ramifications of eating and of obesity in the tribal societies of the past characterized by too little food, and in our contemporary culture characterized by too much food.

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INFLUENCE OF OBESITY ON MORBIDITY AND MORTALITY*

HERBERT H. MARKS

Assistant Statistician, Metropolitan Life Insurance Co.

INTRODUCTION

THE influence of overweight on health is by no means a new subject, but has received increasing attention in recent years. In fact, we are on the eve of the publication of a very large-scale study of mortality in relation to build and blood pressure which will cover the experience of a number of companies over the period 1935 to 1955. Unfortunately, the data of that study are not available for this meeting. Several of the more recent contributions on the subject have come from us at the Metropolitan and have provided new and original data. In this presentation I shall cite, insofar as possible, the latest studies that are pertinent, although many of the good and fundamental investigations in the field are not new and cannot be ignored in any consideration of the subject.

I shall put repeated stress on the relationship of obesity to diseases of the heart and circulatory system. This is warranted by the increasing dominance of these conditions as causes of chronic illness and death. Consider, for example, that last year 55 per cent of the more than one-half billion dollars paid out in death claims by the Metropolitan was accounted for by deaths from cardiovascular-renal diseases. Only 20 years before, the proportion was 43 per cent. Consider also that for white men at age 25, the chances of dying from one of these diseases before age 65 are 16 in 100, out of the total for deaths from all causes of 31 in 100[1].

How do we identify the obese or the overweight? The latter is the term that we much prefer to use. Various measures have been proposed, but for practical purposes in analyzing data on large groups of people, we and others have had to depend, for the most part, on an arbitrary

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definition based upon deviations from average weight for height, age and sex. Admittedly, this leaves much to be desired, but the range of weights and classifications used in our studies is great enough to differentiate the thin, the obese, and various weight subdivisions in between. Until other rapid and reproducible measures are devised, these simple height-weight criteria will continue to serve the purpose.

The available data on the influence or association between body weight and morbidity and mortality are generally in good agreement. The mortality data are far more abundant, more comprehensive, and in many ways, more satisfactory than those on morbidity. Useful data on the relationship of weight to morbidity are largely restricted to those on chronic disorders. The relationship of weight to acute and short-term disorders is rather obscure because their incidence varies so widely and is influenced by so many factors that any effect of weight *per se* would be difficult to isolate and evaluate even if the necessary basic records were available. Moreover, industrial absenteeism records, which form the basis of many morbidity studies, show that a very large part of the short-term absences from work, allegedly due to illness, are ascribed to acute respiratory and digestive disorders and accidents.

Life Insurance Studies of Mortality in Relation to Body Build

Accordingly, I shall present first the pertinent facts from mortality studies. As is well known, they are derived from life insurance experience. The data for them have been collected over a longer period of years and have been periodically analyzed. The volume of data is large and amenable to accurate evaluation. The studies are designed to measure long-range effects. The aim of these studies is by no means academic. It is to determine which groups, if any, classified by build, show sufficient excess of mortality to warrant the charging of extra premiums. This is in accord with insurance practice and policy to assign an equitable rating to each applicant for insurance. Life insurance is a highly competitive business. Comparative costs are closely related to the proper selection and rating of applicants to produce a satisfactory mortality rate in the various classifications of risks. Thus, the attitude of insurance companies with respect to the build of individuals is quite objective.

We may briefly consider the nature and characteristics of the data in these life insurance studies. Applicants are classified either according

to absolute or per cent deviations from average weight for height and age. The initial selection of cases and the subsequent evaluation are entirely independent. The evaluation is based on detailed comparisons of the mortality in each weight classification with the contemporaneous mortality experience on all standard insured risks, i.e., those insured at regular premium rates. These studies generally relate to presumably healthy persons, selected for insurance after medical examination. These persons are in better than average economic circumstances, are free of serious defects and are engaged in safe occupations. In this way major extraneous factors which could influence the results are avoided. Obviously, the cases included in these studies do not represent a cross-section of the population, but are comparable with the standard risks against whom they are measured. To the extent that more serious impairments are more common in overweight persons than in those of lesser weight, the results understate relatively the mortality associated with overweight.

Life insurance studies of mortality in relation to build include three joint investigations[2] to which a number of companies contributed data, and an even larger number of studies by individual companies on their own experience[3]. The first of these studies goes back to the beginning of the century; the latest are concerned with the past decade. While there are differences in detail, the results are consistent in showing that overweight of even moderate degree—say 10 to 20 per cent—is associated with a significant elevation of mortality and that the amount of excess mortality increases with the degree of overweight. Moreover, while in the earlier studies a moderate degree of overweight was found to be advantageous in younger persons, this is no longer true because the disadvantage of underweight existing heretofore has been virtually eliminated as a result of the huge reduction in mortality from tuberculosis and pneumonia, which then were primarily responsible for the high mortality among young underweights.

The many studies are likewise consistent with regard to the causes of death which account for the adverse record of overweights. All of them showed that this is due primarily to excessive death rates from diseases of the heart and circulatory system, diabetes and biliary tract disease. These conditions, and especially heart and circulatory disorders, have come to account for an increasing proportion of total deaths as a result of the decline in the infectious diseases. Accordingly,

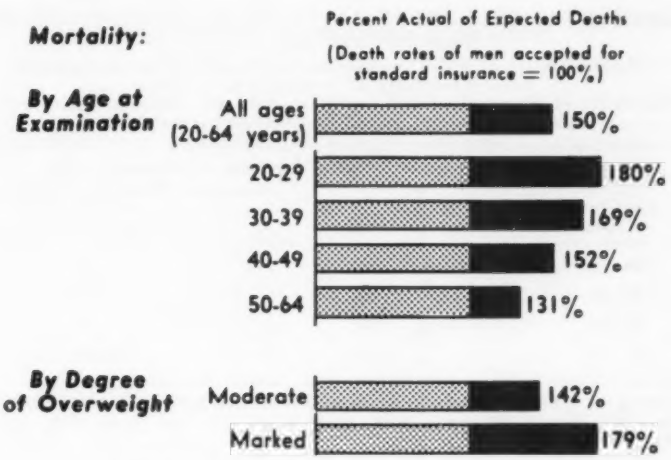


Fig. 1—Mortality of men rated for overweight.
Experience of Metropolitan Life Insurance Company.
Substandard Ordinary Issues, 1925-1934, traced to 1950.

the disadvantage of the overweight as compared with lighter weight groups is relatively more marked than ever before.

Because the general trends in all of these studies are so much alike, it will suffice to show facts from the latest study only[3a]. This was made by the Metropolitan Life Insurance Company and was limited to those applicants accepted for insurance who were charged higher premium rates solely because of their overweight. It covers about 26,000 policies on male lives and 25,000 policies on female lives between ages 20 and 64 issued between 1925 and 1934 and traced to the policy anniversary in 1950. As is customary in life insurance studies, results are reported in terms of the percentage ratio of actual to expected deaths, the expected deaths being computed on the basis of contemporaneous experience among standard risks. I would interject a word of caution about the interpretation of these figures. A ratio of 200 per cent, or double the expected mortality, does not mean a reduction of one-half in the average length of life of a group with such an unfavorable experience. The two measures have no simple and direct relationship. The high ratios do reflect a moderate but often preventable curtailment of longevity, varying according to the degree of excess mortality and other factors.

Figure 1 shows the facts for men, classified according to the age at

TABLE I—MORTALITY AMONG MALES LIMITED TO SUBSTANDARD INSURANCE BECAUSE OF OVERWEIGHT

Observed ratios of actual to expected deaths and estimated ratios on basis of mortality in "optimal weight" group
Experience of Metropolitan Life Insurance Company, Ordinary Department, issues of 1925—1934, traced to policy anniversary in 1950

Age Group at Issue	*Per Cent Actual of Expected Deaths*	
	Observed	*Estimated on basis of mortality in "optimal weight" group**
20—29	180	194
30—39	169	201
40—49	152	197
50—59	131	166

* According to ratios in weight group with lowest mortality in *Medical Impairment Study, 1929*—Ages 20-29—93%; 30-39—84%; 40-49—77% and 50-59—79%. (Ref. 2c, p. 38)

examination for insurance, and by degree of overweight. For the latter, the cases were classified according to our rating standard, which is not based upon absolute or relative amount of overweight. The moderate overweight among the males in the study would average 30 to 35 per cent overweight and among the females 35 to 40 per cent overweight; the marked overweight group would average 10 to 15 per cent higher. It is clear that in all the categories shown, the mortality is significantly elevated. Proportionately, the record among males is worse at the younger than at the older ages at issue. Those who are most overweight show the greatest excess in mortality.

The situation among the overweight women is the same, in major respects, but differs in certain details, e.g., that the relative mortality by age shows no particular trend.

A more rigorous measure of the excess mortality among these overweights is to compare them with weight groups showing the lowest mortality. For this purpose contemporaneous data are not available, but we have made computations, using the mortality in the "optimal weight" class in the Medical Impairment Study, 1929, as a standard. These computations are shown in Table I. On this basis, the mortality ratios among the overweights in this study are of the order of 200 per cent in age groups up to 50, and 165 per cent for those aged 50 to 59 at entry.

Table II shows the relative mortality from principal causes of death

TABLE II—PRINCIPAL CAUSES OF DEATH AMONG MEN AND WOMEN RATED FOR OVERWEIGHT

CAUSE OF DEATH *(Death Rates of Persons Accepted for Standard Insurance = 100%)*	MEN *Per Cent Actual of Expected Deaths*	WOMEN *Per Cent Actual of Expected Deaths*
Principal cardiovascular-renal diseases	149	177
Diabetes mellitus	383	372
Cirrhosis of the Liver	249	*147*
Appendicitis	223	195
Biliary calculi (gallstones)	206	284
Cancer—all forms	*97*	*100*
Leukemia and Hodgkin's disease	*100*	*110*
Tuberculosis—all forms	21	35
Pneumonia—all forms	*102*	*129*
Ulcers of stomach and duodenum	67	*
Suicide	78	*73*
Accidents—total	*111*	135

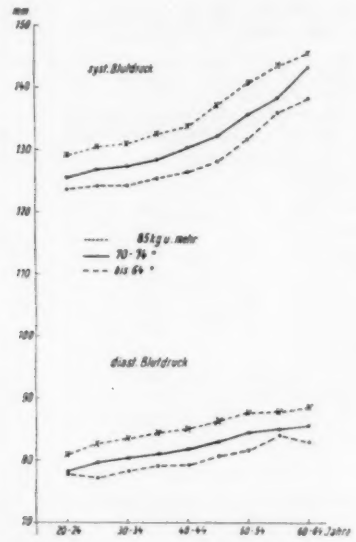
* Deaths too few to warrant calculation of mortality ratio.
Note: Italics denote that the deviation from the Standard is not statistically significant.

Experience of Metropolitan Life Insurance Company. *Substandard* Ordinary Issues, 1925-1934, traced to 1950.

among men and women. This part of the analysis is limited to attained ages 25 to 74. First, attention should be given to the facts for the heart and circulatory disorders because of their outstanding position in the total mortality picture. Among males, the death rate from this group of causes was about one and a half times that among male standard risks, and among females, it was about one and three-quarters times that of female standard risks. Diabetes shows the largest relative excess mortality among the major causes, with a death rate about four times as high as that of standard risks among both men and women. The mortality from cirrhosis of the liver, gall stones and appendicitis was double or more that of standard risks among males and was excessively high among females also. It is notable that although the mortality from cancer in the aggregate was not elevated, the mortality from cancer of the biliary tract was significantly in excess of the expected.

RELATIVE FREQUENCY OF IMPAIRMENTS AMONG OVERWEIGHTS

Studies of the association of overweight with morbidity and impairments are quite numerous but are so heterogeneous in character that it is often not possible to make direct comparisons between them, and



Experience of German Life Insurance Companies, 1955-1956 (Döring)

Fig. 2—Average blood pressure of men, 170-174 cm. tall, in relation to weight and age.

one must be content to ascertain what general tendencies they reveal. These studies differ with respect to the nature and composition of the populations they cover, the duration of observation and the methods of analyzing the data. They are primarily cross-section studies, and in some cases it may be suspected that the weight at the time of observation may not be the usual weight of the individual, and weight reduction has been a part of the treatment he has undergone. This would, of course, primarily affect persons who had previously been overweight. Other biases, often unknown, may exist in the populations studied. Nevertheless, there is a high correlation between the findings in these studies and those in the mortality investigations.

There are numerous studies from widely different sources which show a definite rise in the mean blood pressure levels with increasing weight. I shall cite a few of them, some quite recent. The first large-scale study[4] based upon insurance data was made in this country in 1924 on persons accepted for life insurance, most of them in the decade preceding 1924. Among men between ages 28 and 42, for example, the

mean systolic pressure for those more than 25 per cent overweight was about 7 mm. greater than for those more than 25 per cent underweight. For the diastolic pressure the difference in the means between the two weight groups was about 6 mm.

The recent experience of German life insurance companies is illustrated in Figure 2, and the same characteristics are clearly revealed[5]. The material is based on men 170 to 174 cm. tall, and the averages are given for three weight groups: under 64 kg., 70 to 74 kg., and 85 kg. and over. In every age group the mean figures are lowest for the lighter weight men and highest in the heavier weight group. This applies to the means for both the systolic and diastolic readings.

A study of blood pressure readings on industrial workers collected about 15 years ago showed the same trends[6]. For example, at ages 40 to 44, the mean systolic pressure among men 25 per cent or more overweight was 6 mm. higher than the mean of those 10 per cent or more underweight, and the difference in the mean diastolic pressure was also 6 mm. Even larger differences were found in the case of women, about 14 mm. in the mean systolic pressure and 10 mm. in the diastolic pressure.

A similar study made in Norway on persons examined by plant physicians in 1952 also displayed the same general tendency[7]. The samples for women in some age groups were relatively small, and accordingly, the averages in some detailed weight groups were based on relatively small numbers. At ages 40 to 49 the mean systolic pressure for men 20 per cent or more overweight was 9 mm. greater than for those 20 per cent or more underweight; for women in this age group the difference was 15 mm. The corresponding difference in the mean diastolic blood pressures was about 8 mm. for men and 13 mm. for women.

Another study made in the adult population of two parishes of the city of Bergen, Norway[8], in which the great majority of the population was examined, showed the same general tendency, but this was much less marked than in the other studies. The mean blood pressures for the obese, however, were significantly higher than for persons of lesser weight.

Even in India, according to a recently published study made in Delhi, the blood pressure was found to increase with body weight[9]. Among the men, the data on whom were reported separately for a

rural and an industrial population group and the high socio-economic class, and among women in the rural population, the blood pressure levels, both systolic and diastolic, tended to rise with increase in weight. The number of cases in the various groups was, however, not very large. The association of elevated blood pressure with overweight is found also in the study, quite different in nature, made on Army officers by Levy and his associates[10]. This study was based on long-term follow-up of persons not hypertensive at first observation. Sustained hypertension developed in officers who were overweight at a rate two and a half times as high as in those not overweight.

The recent study by Master and his associates[11] on blood pressure in the elderly shows also that the mean blood pressure readings among the overweights were consistently higher than among middle weight and thin people. This situation prevailed in all groups up to age 80.

The association of overweight with heart disease has been investigated in many studies of different types. Of particular interest are a number of long-range studies which have been started in the last few years in a few communities. The populations covered in these studies are not very large, the periods of observation still rather short and the effects of various biases in the selection of the cases are not known precisely. Time does not permit review of these matters. Nevertheless, the preliminary results are worthy of attention. These studies are concerned with assaying the importance of various factors in the development of heart disease in those who at initial observation had no evidence of heart disease. To date, the most consistent finding is the association of overweight. The study in Framingham[12] is probably best known. There, in the four-year period of follow-up of men between ages 45 and 62, those who were appreciably overweight showed double the frequency of new cases of arteriosclerotic heart disease than those who weighed less.

In Albany, New York, in a study based upon State Civil Service employees 39 through 55 years of age, the incidence of new cases of ischemic heart disease was three times as high in the small group of men 40 per cent or more above ideal weight than in the group as a whole[13]. The incidence is, as yet, little elevated in the intermediate overweight group. A study of Los Angeles Civil Service male employees between ages 40 and 70 has not produced particularly clear-cut results, although the frequency of coronary disease has been higher in the heavy weight

than in the light weight group[14].

The frequency of overweight among cardiac patients seen in private practice was reported by Master and his associates[15]. Among male patients the proportion of overweights was nearly 40 per cent in patients with angina pectoris, coronary insufficiency and hypertension, and nearly 50 per cent in those with coronary occlusion, as compared with approximately 20 per cent in the population used as a control. The findings in females were less clear-cut, but underweight was distinctly less frequent than would be expected among the patients with coronary insufficiency and hypertension.

A further illustration is taken from the intensive morbidity survey made in the Eastern Health District of Baltimore[16]. A special aspect of this was the association of various chronic diseases with overweight. Among patients with coronary disease there was a significantly high proportion of overweights among persons with heart disease.

Diabetes is perhaps the classic illustration of the association of overweight with disease, especially in the type of diabetes occurring in middle life and old age. The great majority of the patients are, or have been, seriously overweight, and a very high percentage truly obese. To take examples from recent studies, I may refer first to the data on 90 industrial workers[17]. Of these, nearly 50 per cent were 20 per cent or more overweight at the time of diagnosis. If the weight before onset were used, the proportion would be appreciably greater. In a recent study in a German clinic[18], 53 per cent of the patients were appreciably overweight according to the standard used.*

The high mortality from liver disorders in the studies of insured overweights is paralleled by their high incidence in clinical experience. A recent study[19] of 20 hospitalized men who were 50 per cent over ideal weight, with no illness involving or likely to involve the liver, showed that six of them had enlarged livers, five had enlarged spleens and four of these had both conditions. Nine of them had impaired glucose tolerance. Moreover, liver function tests were frequently abnormal. In another study of 18 obese patients in a Veterans Administration Hospital, a significant proportion were found to have abnormal liver function tests and a great many had elevated blood sugars on a glucose tolerance test[20].

Gall-bladder disorders also find more victims among overweights

* More than 10 kg. plus height in cm. over 100 expressed in kg.

than among average and underweight persons. This is documented in our insurance experience[21], in the Eastern Health District Study for Baltimore[16] and in an autopsy study at the Mayo Clinic reported by Mentzer[22].

Impairment of pulmonary function in the obese has been the subject of a number of studies, and it will suffice to mention only one recent report[23]. This covered 28 patients who were 100 pounds or more above ideal weight; 15 of them had abnormally low arterial oxygen saturation and 10 of these cases had lung disease. Distinct improvement in the condition was noted when weight was reduced. Even in 13 cases where the arterial oxygen saturation was within normal limits, respiratory reserve volume and mean maximal breath capacity was reduced, but tended to return to normal values in patients who reduced their weight.

Wear and tear on the joints in the body is hastened in some degree by excessive weight. Accordingly, osteoarthritis occurs at a higher rate among overweights than among persons of lesser weight. This is borne out by data from periodic health examinations[24] and by the records of the Eastern Health District Study[16] to which reference has been previously made.

Malignancy of the genital organs, and more especially of the endometrium occurs at a higher rate among overweight women than among those of average weight or less. Several studies have brought this out, notably those by Hertig and his colleagues in the Boston area[25]. Available morbidity data show no other special association of overweight with malignancy, but as already noted, malignancy of the biliary tract is found to be elevated among overweights in the mortality study of insured risks.

Other conditions or symptoms for which there is evidence of greater frequency among overweights than among others include hernia[26], cerebral vascular accidents, peripheral vascular disease[27], and various urinary impairments[28].

Effect of Overweight on Prognosis in Various Disorders

As if it were not enough that overweights are prone to acquire so many impairments and disabilities from so many conditions, especially from serious disorders of middle and later life, the outlook for impaired overweights is usually less favorable than for impaired persons who are not overweight.

The combination of moderate overweight and even slight elevation of blood pressure brings an appreciable increase in the death rate from heart disease. A recent study among persons insured in the Metropolitan Life Insurance Company disclosed a death rate in this group more than double that among standard risks, with arteriosclerotic heart disease being responsible for most of the excess mortality. In cases with a moderate elevation of blood pressure, the mortality from heart disease was even higher. In the Framingham study likewise, the combination of overweight and hypertension was found to have a greater adverse effect on the incidence of arteriosclerotic heart disease than either factor alone. Again, in the study of Army officers by Levy and his associates[10], the overweights with a history of transient hypertension and tachycardia developed sustained hypertension at a rate one and a half times as high as in those not overweight.

Our insurance studies have disclosed several other groups in whom overweight is an adverse factor, as shown by the excess in mortality among impaired overweights with such conditions as asthma[29], bronchitis[30], albuminuria[31], and high blood sugar[32].

The overweight surgical patient apparently offers special problems both to the anesthesiologist and the surgeon, although what this means in terms of extra morbidity or mortality has not been well documented. Schwartz has recently summarized these problems from the point of view of the anesthesiologist[33]. He cites difficulties in maintaining a free airway, inadequate respiratory exchange, longer induction and recovery periods, and need for greater muscular relaxation. He also refers to the problems arising from the more frequent occurrence in overweights of cardiovascular disease, diabetes and abnormal liver function. Specific evidence of surgical problems in overweights is the increased frequency among them of postoperative embolism and thrombosis. Barker and his associates[34] reported that in female patients weighing over 200 pounds who underwent abdominal hysterectomy or intestinal operations, this occurred at about double the rate found in those women undergoing the same operative procedures who weighed less than 200 pounds.

The overweight woman runs extra risk from pregnancy, and her chances of bearing a live and healthy child are diminished, especially if she has been in difficulty in a previous pregnancy. Thus, a number of studies all indicate a higher frequency of complications during pregnancy and delivery and an increase in both maternal and fetal mortality[35]

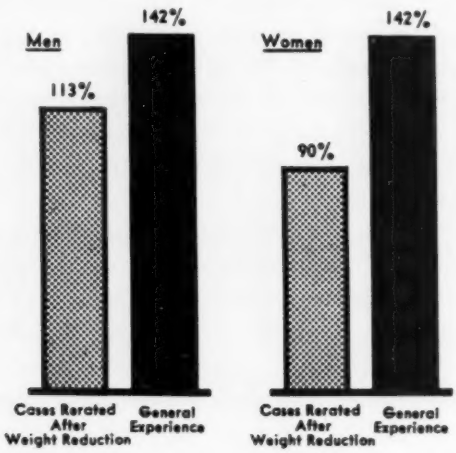


Fig. 3—Effect of weight reduction on mortality. Experience on persons rated for moderate obesity who received lower ratings after weight reduction compared with general experience on cases rated for moderate obesity.

Experience of Metropolitan Life Insurance Company.
Substandard Ordinary Issues. 1925-1934, traced to 1950.

More overweight women tend to have large babies than other mothers and a relatively high proportion of them eventually develop diabetes[36]. In women with a history of eclampsia, toxemia developed in a subsequent pregnancy in 75 per cent of the overweight women, as compared with 26 per cent in women of light build, according to a study by Chesley and his associates[37].

Effects of Weight Reduction on Mortality and Prognosis in Overweights

The question then naturally arises: What benefits ensue to overweights if they reduce? There is evidence that weight reduction brings improved health and longevity to many, although comprehensive and long-term measures of this result are difficult to obtain. The best overall evidence to date has been derived from the study of persons in the Metropolitan Life Insurance Company who were rated, i.e., charged extra premiums, merely because they were so much overweight[38a]. A group of cases in this study were identified who later reduced their

weight and maintained it sufficiently long so that the rating was removed. The experience on these cases is shown in Figure 3. In this group of both men and women, the mortality was substantially less than in the general experience among overweights. The rate of decline in mortality from cardiovascular diseases was apparently as great as that from all causes, although we could not determine this exactly.

A number of scattered studies based upon clinical experience show the benefit of weight reduction in various conditions. Weight reduction is now an orthodox part of the treatment of hypertension, and several studies have shown a lowering of blood pressure following weight reduction. This matter was carefully re-investigated recently by Martin[38] in England, in a series of 37 obese patients of whom 18 had normal blood pressures and 19 had hypertension. These patients did not suffer from chronic nephritis, malignant hypertension or valvular heart disease. They had remained on a reducing diet and had lost at least 14 pounds during a period of observation of at least six months. The reduction in blood pressure was considered significant only if it reached or exceeded 20 mm. in the systolic level or 15 mm. in the diastolic level. By this criterion, significant lowering of systolic pressures among the hypertensives was obtained in five of the 19 hypertensive cases, and in two patients both systolic and diastolic levels were reduced. In the 18 cases with normal blood pressure, the systolic pressure was lowered in three and both levels were lowered in one additional case. While this response is not extraordinary, the author concluded that the occasional successes obtained, coupled with the subjective improvement in the majority of cases, justified the continuance of weight reduction as a routine measure in obese hypertensive patients, and that benefit was also obtained by lowered demands made on the heart in these hypertensive cases.

Another illustration is the finding, reported by Lups and Francke[39], that during the period of starvation in wartime Holland (September 1944 to May 1945), a reduction in blood pressure frequently occurred in association with weight loss, especially in hypertensive patients.

Treatment of the overweight cardiac patient includes weight reduction but, to my knowledge, no studies have been made of the long-term prognosis in obese cardiacs who have successfully reduced as compared with those who have not. The purpose and value of weight reduction would seem to lie in cutting down on the amount of work performed

by the heart in these patients. Obviously, however, body weight is only one factor in the prognosis of the cardiac patient.

Middle-aged overweight diabetics have shown a return to normal glucose tolerance with reduction in weight. Newburgh[40] demonstrated that where the weight was brought down to the normal level, normal glucose tolerance was restored in nearly 75 per cent of the cases, and improved tolerance was observed in half the remaining cases, as well as in some patients with lesser degrees of weight reduction. Osserman and Dolger[41] obtained roughly comparable results with obese diabetics whose weight was reduced.

A recent study by Goodman of 135 elderly obese patients in a Cleveland Nursing Home in whom diabetes, gangrene, congestive heart failure and cerebral vascular accidents were in excess of the expected number showed that beneficial results were always seen with weight reduction[27]. In 75 per cent of these patients the blood pressure was above 150/90, and the blood pressure levels almost invariably fell with weight reduction.

Summary

We may briefly summarize by pointing out that a wide variety of data from many different sources indicates that overweight impairs both health and longevity. It is associated with an increased frequency of many serious disorders, most important of which are those involving the heart and circulation. These are precisely the conditions which today are responsible for a majority of all deaths and probably even of premature deaths. Overweights in whom serious disorders have developed do not live as long as thinner people similarly impaired. Nevertheless, some improvement in the prognosis for overweights with serious disorders may be achieved by weight reduction.

Addendum—The new study on mortality according to build to which reference was made has since been completed and published (Build and Blood Pressure Study, Society of Actuaries, Chicago, 1959). As in earlier studies, the mortality of overweights exceeds that of lighter weight persons and increases with degree of overweight. The major difference between the new and the earlier studies is that the mortality rate of overweights has become higher in comparison with that of underweights. The former disadvantage of underweights, especially at the younger ages, due to their high mortality from tuberculosis and pneumonia, has been virtually eliminated by the radical reduction in mortality from these diseases. In contrast, cardiovascular diseases, from which overweights experience above-average mortality, have steadily increased in proportion to the total mortality and now account for a majority of the total.

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THE PATHOLOGY OF OBESITY*

W. STANLEY HARTROFT

Mallinckrodt Professor and Chairman, Department of Pathology, Washington University Medical School; Pathologist-in-Chief, Barnes and Allied Hospitals and St. Louis Children's Hospital, St. Louis, Missouri

OBESITY is an abnormal accumulation of fat in the adipose tissue depots of the subcutaneous tissue and mesenteries as well as a number of other important sites associated with the connective tissue capsules and septa of many of the abdominal and thoracic viscera. Although the etiology of obesity is ill-understood, its pathogenesis clearly consists of a chronic increase in caloric intake over caloric expenditure. The resulting net gain in calories is stored in the form of excess fat in adipose tissue. Moderate stores of fat are obviously desirable in a physiologic sense and only those which can be regarded as abnormally excessive produce the condition of obesity. Accordingly, a quantitative element comes into the definition of obesity. The consensus of many authors is to define obesity as that state where the weight for specified heights, ages and sex is 10 per cent or more over that defined as "ideal" [1, 2], and where most of this overweight condition is due to adiposity[3]. It is not our intent to discuss further these quantitative aspects of the question but to describe some of the qualitative pathologic changes associated with obviously obese states.

Abnormalities in the amount and distribution of fat deposits have been variously classified by pathologists. It is our intent to discuss only the first type listed below—*Adiposis simplex* or simple obesity. But for the sake of completeness, a typical list of pathologic obese states are given.

Adiposis simplex.

Adiposis dolorosa (Dercum's disease, 1892) (Lipomatosis neurotica)

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is a state characterized by excessive development of adipose tissue over the upper trunk, neck and axilla which is tender and painful. It is further characterized in some pathologic descriptions as associated with inflammation of the nerves supplying the adipose tissue plus similar involvement of the sympathetic nerves. Pigmentation of the areas with ulceration, loss of hair and vasomotor instability have also been noted. The condition is usually said to affect females past the menopause; it is rare, little understood and may not constitute a true entity.

Madelung's disease (1888) refers to a diffuse symmetrical lipomatosis of deposits of fatty tissue on the upper part of the back, shoulders and neck. Sometimes the condition is restricted to the neck-region and is then called Madelung's "fat neck".

Adenolipomatosis is used to refer to general or local deposits of excess adipose tissue infiltrated microscopically with lymphocytes. The condition is also referred to as nodular lipomatosis.

Steatopygia is a special condition encountered in African Bushmen tribes, particularly the women. It is apparently an hereditary or racial condition in which, under favorable dietary conditions, excessive fat is laid down, primarily over the buttocks, producing bizarre gluteal humps.

Adiposa tuberosa simplex of Anders (1908) refers to a condition characterized by the appearance of multiple lipomas.

Sclerema neonatorum is a rare disease of infants in which the stored fat is chiefly palmitic and stearic with little oleic fatty acid. The adipose tissue has the consistency of tallow. The disease is rare, of unknown etiology and is most likely related to an hereditary defect in enzyme systems connected with fat breakdown, transport or synthesis.

Other abnormalities of adipose tissue include the various lipodystrophies, but these are not forms of obesity.

None of the above conditions is of great practical importance in terms of public health, except for the first—simple obesity as it is recognized by both the physician and the layman. The rest of this discussion will concern itself solely with the pathologic implications of this condition.

Normal Storage of Fat

The term *pathology of obesity* implies that it is an abnormal state. Such a viewpoint is, however, peculiar to our Western civilization only in the past century or two. In more primitive societies or in cultures where food was not plentifully abundant as it is in our times in America, obesity was the mark of the successful man who had perhaps wisely laid down body stores of calories upon which he could draw in times of general famine or personal disaster. As Goldner[4] puts it, ". . . obesity was considered a sign of health and vigor, of beauty and respectability and of wealth and trustworthiness".

From the physiologic standpoint, it would surely seem beyond debate that at least moderate stores of fat in adipose tissue depots are, even today, desirable in order to provide a ready source of calories that can be mobilised in times of illness, when the normal caloric intake may be impaired because of digestive disturbances, or when caloric expenditure is elevated above normal because of increases in metabolic requirements associated with the hyperpyrexia, etc., of infectious states.

With these points in mind, one might more accurately speak of the *histology* of obesity and then enquire whether or not the storage of large amounts of fat in adipose tissue is associated with pathologic states. Mr. Herbert H. Marks* has already presented statistical data relevant to this last question. In the latter portion of my contribution, I shall deal with some of these aspects from the standpoint of morbid anatomy. The site of storage of fat in obesity is properly in adipose tissue. But this accomplishment is the normal function of adipose tissue, and as long as the excess lipid is deposited *only* in these physiologic storage depots, the process *per se* can scarcely be termed pathologic—even when proceeding to relatively extreme degree. As we shall see, however, in some instances excess fat may sometimes be deposited in other tissues—such as heart, kidney and liver. Here one might draw a qualitative distinction between physiologic storage in adipose tissue and pathologic accumulation in other tissues and organs. The latter is associated not only with obese states but also with a number of other dietary, hormonal or circulatory abnormalities.

Fat cells distended with stored lipid to the greatest degree are found in groups forming lobules around vessels, particularly in subcutaneous tissues, mesenteries, the deeper connective tissue around the kidneys,

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around the pancreas and between its secondary lobules and lobes and around the heart. Adipose tissue is formed as early as the fourth month of gestation in human embryos[5]. Although the cells at first resemble surrounding fibroblasts, the presence of lipid-containing vacuoles differentiates them from the latter. As the cells differentiate, the vacuoles fuse together forming one large drop, displacing the nucleus to one side and producing the familiar "signet ring" cell. Present evidence indicates that adipose tissue is a true tissue and not merely a collection of fibroblasts which happen to contain fat.

In mature adipose tissue, the large fat-distended cells are supported by partitions of collagenic and elastic fibers; fibroblasts, macrophages and mast cells are present in it. There is a rich capillary network supplying the adipose tissue cells, and injection studies indicate that a capillary lies on some aspect of every cell.

Studies of transplanted fat-grafts indicate that as fat is deposited in adipose tissue, the individual cells become distended with the lipid, but few new cells are formed. On the basis of these and other studies, it is believed that accumulation of fat in adipose tissue of adults is not accompanied by hyperplasia of cells (increase in number) but by hypertrophy (increase in size) of pre-existing cells that previously contained only a few cytoplasmic vacuoles. The so-called *brown fat* of the intercapsular gland is rich in glycogen as well as fat and appears to be a special type of tissue lying outside the scope of this paper. In man, brown fat may give rise to the special form of lipoma known as a hibernoma[7].

In very obese rats, we have observed[8] fusion of adjacent adipose tissue cells into fatty cysts similar to those we have previously described as forming in the liver from hepatic cells that have been subjected to excessive accumulation of fat[9]. In some instances, associated with subsequent weight reduction in the animals, the cells forming walls of atrophic cysts in adipose tissue have numbered as many as 50 to 60 in single sections. We do not know yet whether fat stored in this form (in fatty cysts in adipose tissue) is as easily mobilised during periods of caloric restriction as is fat stored in the usual way in individual cells. During periods of emaciation, single fat cells undergo a reversal of the steps observed during their accumulation of lipid. They become small; their cytoplasmic rims thicken; each cytoplasmic fat-drop breaks into smaller droplets or vacuoles and the nucleus may move to a

more central position. A reticulum appears between the shrunken cells, some of the fibers appearing to originate from the atrophic fat cells and others from scattered, intervening fibroblasts and fibrocytes.

Abnormal Fat Storage

Virchow originally described two types of abnormal fat storage—fatty infiltration and fatty degeneration. The former process is uniquely associated with obesity and affects the heart and exocrine pancreas *especially*. The fat-laden adipose tissue surrounding these organs in the obese individual frequently encroaches between their structural units. In the pancreas, the lobes and secondary lobules are widely separated and, indeed, the acinar tissue is often reduced and replaced by bands of adipose tissue. It would be tempting to correlate this pathologic alteration of the pancreas with the frequent association of diabetes with the obese state, but the islets appear resistant to this type of infiltration and replacement. Several studies have indicated[10] that despite the high content of fat in these pancreases, their islet-numbers and insulin-content usually fall within the range of values for comparable non-diabetic controls. In the case of the heart, adipose tissue grows between the muscle bands, particularly of the atria, and less frequently, of the ventricles. Weakening of the myocardium by this process to the point of rupture has been proposed, but in our experience more profound pathologic changes, such as infarction, must be present in addition to fatty infiltration before the latter process alone can so alter the heart that rupture results.

The second type of abnormal fat storage in obesity—accumulation of fat in parenchyma, rather than infiltrating adipose tissue cells—is exemplified by the liver. Fat people, both diabetic and non-diabetic, generally have fatty livers[11]. This form of abnormal fat storage within the hepatic cells is sometimes referred to as fatty degeneration, but we believe the term implies more than is warranted. Aside from the presence of the fat, there is often little evidence that degeneration of the affected cells is actually present. For this reason, the more non-committal and purely descriptive phrase of simply abnormal fat storage seems preferable. In this laboratory, we have obtained corroborative evidence of the studies in obese man and have shown that in various forms of experimental obesity in rats and mice a special type of fatty liver develops.

Experimental Observations on the Liver in Obese Animals

Rats were rendered obese by several different methods. Insulin injections given daily increased their appetite and their food intake appreciably over saline-injected controls. A much greater degree of obesity followed the production of hypothalamic damage[12]. Mice became obese when given gold thioglucose at a level of MLD_{50} and their livers were similarly studied. In the rats, all types of increased caloric intake were followed by an increase, biochemically and histochemically, of hepatic fat. The form in which the lipid accumulated in the liver was quite distinct from that seen in choline deficiency in the same species[8]. Choline supplements up to 1.0 per cent of the diet were ineffective in preventing these fatty livers in the obese rats. The fat was deposited consistently in the periportal regions of the hepatic lobules, whereas that associated with choline deficiency is always centrolobular. Fatty cysts, formed by the fusion of adjacent fat-distended hepatic cells, are a prominent feature in centrolobular regions of choline-deficient rats, but were much less frequently encountered in the fatty livers of fat rats. In the latter animals, fat distended individual periportal cells to enormous degrees, enlarging them to diameters of almost 100 micra or more (compared to diameters of 7 to 10 micra in comparable sections of livers of control rats). The fat, however, did not form large intracytoplasmic globules as it regularly does in choline-deficient animals, but remained as innumerable discrete droplets throughout the cytoplasm of the cell. The cells, despite the large amount of fat present within them, retained their polygonal shapes. The nuclei were not often displaced to one side when the liver cells had accumulated their fat in the obese animals as was so regularly observed in the choline-deficient ones. In several ways, the fatty liver of obesity therefore differs sharply from that of lipotropic deficiency. On the other hand, accumulation of hepatic fat in cachectic and diabetic animals resembles, somewhat pardoxically, the liver of obesity because its distribution in all these states is periportal, contrasting with the centrolobular type of fatty liver in choline deficiency. These findings suggest that different enzymatic pathways present in the two portions of the liver lobule are altered specifically in the various types of fatty liver (central *vs.* portal).

In mice given gold thioglucose, fatty livers also developed and

choline supplements were equally ineffective in preventing them. In this species, however, the fatty livers associated with increased caloric intake were centrolobular. These differences in distribution of the fat pose a challenging problem to the investigator.

In none of the above experiments did the abnormal accumulation of hepatic lipid produce either hepatic fibrosis or cirrhosis, both of which regularly follow the fatty liver of choline deficiency in rats, mice and other species. In man, cirrhosis has been reported to be two and a half times as frequent in the obese adult male than in his non-obese counterpart[13]. But it has also been found that abnormalties of the gall bladder and bile duct are more frequent in the obese than in the non-obese[14], and this factor may be more important in the pathogenesis of the cases of cirrhosis than the accumulation of fat within the liver. In animals, at any rate, we have not been able to produce cirrhosis through over-feeding, despite the production of fatty livers. In man, other factors, such as diabetes and/or alcoholism, may act in association with obesity as epidemiologic factors in the associated cirrhosis.

In all the animal studies cited above, the cardiovascular systems were carefully searched for atherosclerotic changes, but none were found. In this respect, earlier investigators who met with similar negative findings have been confirmed[15].

In both animals and man, abnormal forms of fat storage can be demonstrated in obese states. These lesions include unusual forms of storage within the adipose tissue *per se* (adipose tissue cysts); infiltration of other organs (heart and exocrine portion of the pancreas) by adipose tissue and abnormal storage of fat in other organs, most notably the liver. Despite the frequency of these structural alterations in obese patients coming to autopsy, the changes do not correlate well with the presence or absence of diseases frequently associated with obesity by the clinician and the statistician. The remainder of this discussion will examine the relationship between obesity and two conditions frequently associated with it—namely hypertension and myocardial infarction as encountered in the autopsy room.

Obesity, Hypertension and Myocardial Infarction at Autopsy

There is excellent evidence from a number of sources that the frequency of diabetes in the obese adult is three to four times the rate expected in comparable non-obese adults[13, 16]. Evidence is equally con-

clusive that hypertension and myocardial infarction are more frequently present in the diabetic than in the non-diabetic. It is obvious, therefore, that they will be more frequently encountered in the obese as an entire group. But in our autopsy investigations, we have not found a similar association between either hypertension or myocardial infarction and obesity in non-diabetic adults[17, 18].

The average body weight of adults of both sexes dying of *recent* myocardial infarcts was 65 kg. Because it might be argued that they had lost appreciable amounts of body weight between the onset of their symptoms and death, controls consisted of a group of patients that had been subjected to neurosurgical operations (other than in the region of the pituitary or hypothalamus) and died within two weeks. The average weights of the latter, matched for age and sex, were 63 kg. Differences were not statistically significant. Diabetics were not included in either group. These data, obtained from cases of recent, *proven* myocardial infarction, do not therefore support the clinical or statistical data presented earlier. It is our feeling that the obvious difficulties of accurate diagnoses in extremely obese individuals may make antemortem data somewhat open to question.

In a sister study[18], the question of hypertension and its frequency in non-diabetic obese patients was investigated. Combined weights of both kidneys removed from known hypertensive patients at autopsy weighed 278 gms., 97 gms. less than non-hypertensive controls matched for age, sex and weight. These data established that the kidneys of hypertensive patients coming to autopsy were significantly smaller than kidneys of non-hypertensive patients.

But kidneys of 56 patients coming to autopsy with both the clinical and necropsy diagnosis of obvious and extreme obesity (adiposity) weighed 345 gms. whereas those of 56 non-obese controls weighed 312 gms. These data suggest to us that hypertension in these obese patients was not sufficiently common to be associated with a significant reduction in their renal weights, although this was true in control groups of proven hypertensive patients of all ranges in weight. Again we feel that methods of assessing the presence of hypertension in obese patients during life may be open to question—at least until the use of specially wide cuffs or more direct types of measurement of blood pressure are more commonly adopted.

Our purpose in presenting briefly the negative results of the above

two studies has not been merely to stir up a controversy, but to emphasize the need for still closer examination of data. There is little room for disagreement that extreme degrees of obesity are undesirable from the standpoint of public health and preventive medicine. Recent documentation of cardiorespiratory dysfunction and polycythemia in patients with *extreme* obesity illustrates at least one very clear functional disability and syndrome resulting from incomplete respiratory excursion and aeration[19] secondary to excess fat deposition within and around the thoracic cavity. Diabetes is probably the most conclusively demonstrated hazard linked to obesity in those individuals with a genetic predisposition to the disease. In the absence, however, of a basic metabolic defect in fat transport and metabolism, such as exists in diabetics, we believe the data concerning the ill effects of mild degrees of obesity may have been somewhat exaggerated during the past decade. Teleologically, a mild degree of obesity (not more than 20 per cent greater than an "ideal" weight) should enable the individual better to withstand sudden periods of caloric deprivation in acute illnesses or following accidents. In states of nutrition not exceeding this degree, the pathologist does not encounter the abnormal forms of fat storage described in the earlier parts of this paper. He is therefore unable to speak of the pathology of obesity when limited to this extent. In extreme forms, the pathogenic link with diabetes and its associated lesions becomes obvious; fatty infiltration of heart and pancreas may be extreme, the fat in the adipose tissue *per se* may be held in an unusual, if not abnormal, manner and the liver is almost invariably the site of abnormal deposition of lipid in periportal regions. Perhaps with the advent of more precise tools and their application to the autopsy procedure, the pathologist will be able to detect true pathologic changes in mild stages of obesity. But, at present, lesions can only be linked to the advent of diabetes or to stages of obesity where sheer mechanical embarrassment from overcrowding produces organ dysfunction and provides correlation with clinical findings associated with excessive adiposity.

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GENETIC FACTORS IN OBESITY*

JEAN MAYER

Associate Professor of Nutrition, Department of Nutrition,
Harvard School of Public Health, Boston, Massachusetts

CONTROL of obesity will be established on a rational basis only when we understand the normal mechanism of regulation of food intake and the various ways in which such mechanism can be interfered with. At present a tentative scheme of regulation of food intake has been presented as a result of recent experimental work conducted in this writer's laboratory[1-3]. The regulation would rest essentially on the fact that the ventromedial area of the hypothalamus possesses very special metabolic properties which render it quite different from other parts of the brain, including adjacent parts of the hypothalamus. It is, in particular, different as regards rate of absorption of glucose, phosphate and potassium, with this absorption being sensitive to the state of nutrition of the animal[4]. Levels of blood glucose and of hormones, in particular insulin, may affect passage of glucose into the cells[5]. The ventromedial area appears to act as a satiety block on a more lateral area of the hypothalamus[6, 7], which in turn is relayed to cortical function through projections, parts of the path of which are known but the greater parts of which are unknown. The thalamus and the frontal lobes appear involved. The ventromedial area controls, in part, gastric contractions, presumably through the descendant Schutz's bundle which goes down to the roots of the vagus and through the vagus to the stomach, with consciousness of gastric contractions being relayed back to the brain through the splanchnic nerve[2, 3]. It is apparent that this mechanism is vulnerable to any dysfunction of the hypothalamus and to the nervous centers, in particular through any disturbances in the acid-base electrolyte balance, etc. It is also vulnerable to any disturbances

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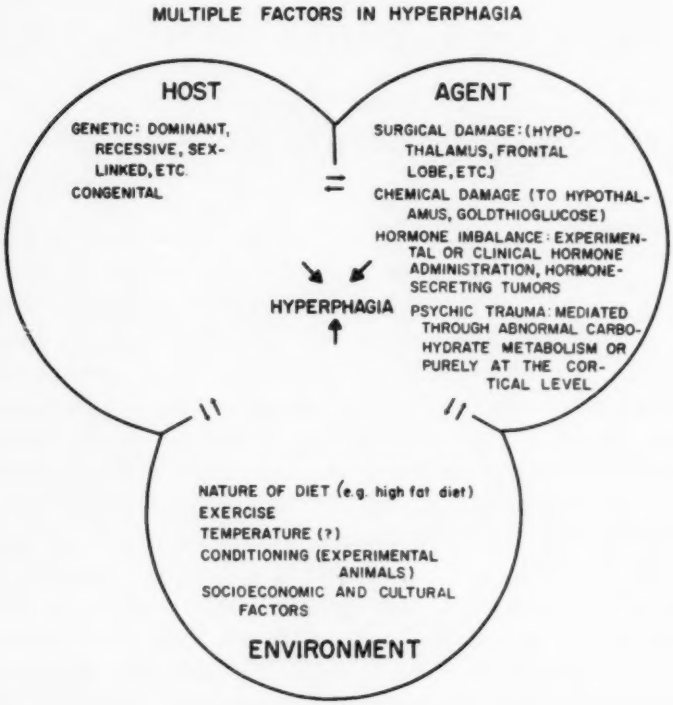
MULTIPLE FACTORS IN HYPERPHAGIA
HOST
GENETIC: DOMINANT, RECESSIVE, SEX-LINKED, ETC.
CONGENITAL
AGENT
SURGICAL DAMAGE: (HYPOTHALAMUS, FRONTAL LOBE, ETC.)
CHEMICAL DAMAGE (TO HYPOTHALAMUS, GOLDTHIOGLUCOSE)
HORMONE IMBALANCE: EXPERIMENTAL OR CLINICAL HORMONE ADMINISTRATION, HORMONE-SECRETING TUMORS
PSYCHIC TRAUMA: MEDIATED THROUGH ABNORMAL CARBOHYDRATE METABOLISM OR PURELY AT THE CORTICAL LEVEL
HYPERPHAGIA
NATURE OF DIET (e.g. high fat diet)
EXERCISE
TEMPERATURE (?)
CONDITIONING (EXPERIMENTAL ANIMALS)
SOCIOECONOMIC AND CULTURAL FACTORS
ENVIRONMENT

Fig. 1

in the endocrine balance affecting carbohydrate metabolism and to any abnormality in the metabolism of adipose tissue, in particular as it relates to fat synthesis of mobilization and, directly or indirectly, affects carbohydrate removal from the blood. Finally, as the unconscious or subconscious impulses from the lower part of the brain have to be interpreted and acted upon by the cortex, the system is also vulnerable to a whole series of psychic factors[8, 9]. It has also been shown that the mechanism of regulation of food intake is not a perfect one in the whole range of energy expenditure. When levels of energy expenditure are low, food intake is not correspondingly decreased; in fact, it may be increased, with positive balance the result[10-12]. Similarly, it appears that the ability to switch from a high carbohydrate to a high fat diet without putting on extra weight is not perfect in all strains. It has been shown by

Fenton and his collaborators that certain strains of mice are unable to make that switch without considerable accumulation of fat[13, 14]. A similar finding has been reported for certain strains of rats, a result which illustrates the interaction of constitutional and environmental factors in determining adiposity[15].

Any mechanism which is that complicated can obviously go wrong in a great many places. Factors leading to obesity have been classified according to the classic epidemiological concept of the trinity of host, agent, and environment. Genetic, traumatic, and environmental factors can thus be described and distinguished[8]. Figure 1 gives illustrations of interaction of such factors in producing hyperphagia. A more extensive description of examples of the different types is to be found in previous reviews[8, 10, 16]. Causes of obesity can also be described in terms of mechanism (pathogenesis) rather than in terms of primary factors (etiology). The discussion which follows will endeavor to use some of the examples of experimental obesities worked out in mice, particularly genetic obesity and goldthioglucose hypothalamic obesity as illustrations of the difference between the types of obesities due solely to a primary hyperphagia and those where a lesion in the metabolism is the primary factor, with hyperphagia the more or less distant consequence.

* * *

It is rather amusing that, while misinformed public health educators have denied the importance of genes in the determination of obesity, farmers have recognized and utilized this genetic determination for thousands of years. When animal fat is desired, certain strains predisposed to adiposity are selected in preference to other strains. Laboratory studies offer an even more convincing example of the influence of genetic factors in the development of obesity. In the mouse, in particular, the hereditary obese-hyperglycemic syndrome, the yellow obesity and the New Zealand form of obesity offer striking illustrations of genetic obesity.

The obese-hyperglycemic mutation arose in the summer of 1949 in the V stock of the Jackson Memorial Laboratory[17]. It is a recessive gene. Unlike the yellow mice, there is no external characteristic which makes future obese mice recognizable at birth. The weight gain is not unusual during the first four weeks. The weight of the obese animals (one mouse out of four on the average) then continues to increase

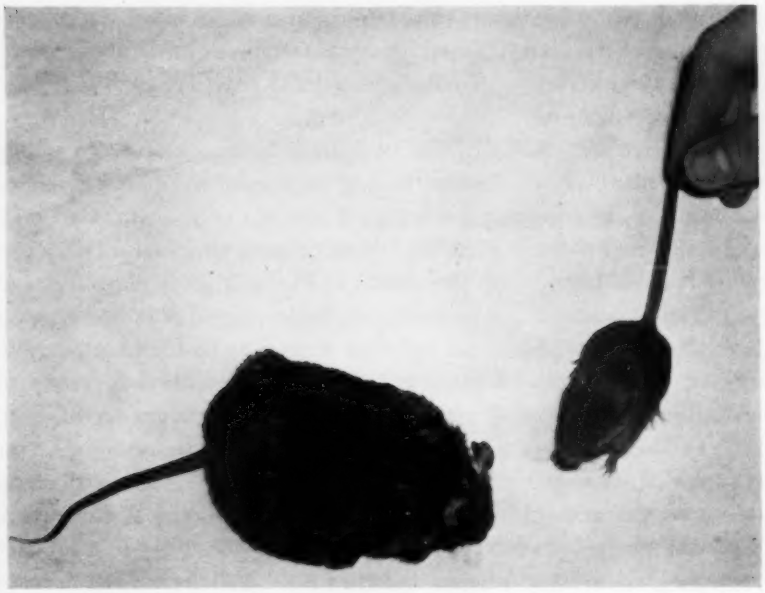

Fig. 2—An obese-hyperglycemic mouse with non-obese littermate.

rapidly, while that of the non-obese mice (one out of three of which carries the obese gene) tapers off. At three months, the weight of the obese mice can be twice that of the non-obese siblings. The highest weight recorded for an obese-hyperglycemic mouse in our laboratory was 119 gm. (Figure 2 shows this animal, at that time weighing 115 gm., and her sibling, weighing 24.5 gm.) The V stock is extremely heterogeneous, so that the colors, size and many other characteristics of the obese-hyperglycemic mice vary quite widely from animal to animal. The obese mice do not mate. This is not due simply to their obesity as such: non-obese littermates of obese-hyperglycemic mice made obese by hypothalamic lesions due to goldthioglucose administration, mate, raise litters and nurse them[18]. Actually, though the gonads of both male and female obese-hyperglycemic mice are somewhat smaller than those of their normal littermates[18], histologic appearances are normal[19]. Runner and Gates[20] have conducted transplantation experiments in which the eggs were obtained by administration of gonadotropic hormones and

then transplanted for gestation in unrelated fostermothers. All resulting individuals carried the obese gene. Lane and Dickie limited the food intake of male obese-hyperglycemic mice to 3 to 4 grams and thus restricted their weight to 26-30 gm.[21] (Such a procedure, as will be pointed out below, does not prevent the mice from being obese from the point of view of body composition. In that range they still contain three times as much fat as non-obese mice of the same weight[22]. On the other hand, though still present, the obesity is of course far less marked than in unrestricted mice: 70 gm. obese mice contain over 20 times the fat content of non-obese 30 gm. littermates[23].) When the adiposity is restricted to that extent, the males, at any rate, mate: the average litter-size was six or seven[21].

Unrestricted mice have been shown to have a striking increase in fat content, the excess weight being almost entirely fat .Total body water increases only slowly with body weight. The proportion of excess body weight represented by water is of the order of 10 per cent as determined by deuterium dilution[24], less than 10 per cent as determined by chemical analysis[25]. Total body protein content is not increased. Blood volume is not increased. Muscles and liver show some degree of intracellular dehydration and a greater degree of extracellular dehydration without change in concentration of intracellular potassium[26]. The fat content is high even in very young animals. Twenty-seven gram obese mice contain ten times as much fat as 17 gm. non-obese littermates[25]. The fat is centrally located, causing at least 50 per cent increase of abdominal girth over normal, 25 per cent increase in thoracic girth and 20 per cent in neck circumference. The size of the extremities and face is not abnormal. Obese animals not infrequently show areas of denuded skin, particularly at points where the skin rubs against the cage or feeding cannisters. These areas are inelastic and wrinkled. Particularly if skin parasites are present—a situation much more likely to develop in obese animals which have difficulty in grooming—they may present in their center punched-out ulcers with bases of lobular, glistening yellow-white subcutaneous fat and ragged margins of thin skin[19].

Organ sizes illustrate the fact that in obesity we may find some specific alterations which may be part and parcel of the syndrome of which obesity is also a part (especially in "metabolic" obesities) and nonspecific effects of hyperphagia and extreme adiposity. Obese-hyperglycemic mice show enlargement of the liver, gastrointestinal tract,

heart and kidney. These changes, also found in the "regulatory" gold-thioglucose obesity, appear to be nonspecific and to be the result of increased food intake, whatever its cause. By contrast, specific changes are also noted in the hereditary obese-hyperglycemic syndrome: the pancreas and thymus are enlarged both in young and in adult animals. The adrenals are enlarged in older adults. The brain is slightly decreased in size, with the decrease being essentially in the frontal and olfactory lobes. The uteri are decreased in size in older animals[18].

Microscopically, the pituitaries appear to contain basophils and acidophils in number comparable to that of the non-obese mice, with no adenomatoid collections of cells, necrosis of cells, Crooke's changes of the basophils, variations in cell sizes, basophilic "invasion" of the posterior lobe or hyaline plaque being observed. The microscopic appearance of the adrenals is not markedly abnormal, though the distribution of adrenal lipoid is reminiscent of the pattern observed in immature mice or of mice younger than the obese animals under examination. Peripheral eosinophil counts are normal. The hearts, lungs and livers are normal. The central nervous system appears normal (with the exception of the decreased frontal and olfactory lobes). The neurons at the hypothalamic, spinal, cervical and low dorsal levels appear normal[19].

The most remarkable abnormality is the increase in vascularization of the pancreas (which probably accounts for the pinker hue of the whole organ) and the increase in size of the islets of Langerhans[19, 27, 28]. Quantitative determinations show that the number of beta cells is increased to a greater extent (approximately 6 times) than the number of alpha cells (approximately 3 times). Mitotic figures are much more frequent than in non-obese siblings. Some of the islets show a definite trabecular pattern similar to that observed in regenerating islets. Neoformation of islets seems to take place at the end of secretory ducts. It appears that formation of islet tissue also takes place from acinar cells. The beta cells show either degranulation with a spread to the whole cells of the tint usually limited to the beta granules or large, confluent, stained masses rejected to the periphery of the cells.

Obese animals eat, on the average, 20 to 30 per cent more than non-obese animals[29]. The feeding pattern is quite unlike that of their non-obese siblings: these show a 24 hour cycle where a prolonged period of satiety alternates with a period of rapid eating. By contrast, the obese-hyperglycemic mice show a number of alternating periods of satiety

and rapid eating in the course of the day; these appear more marked than in hypothalamic mice, whether the lesions are inducted by goldthioglucose or by stereotaxic means[30].

There are other differences with non-obese littermates made obese by hypothalamic lesions (caused in particular by goldthioglucose administration). Such animals are very hyperphagic (50 to 100 per cent greater intakes than normal). Their activity is as high as that of normal animals and their oxygen consumption increases in proportion to their body surface[31], unlike that of obese-hyperglycemic mice[32]. It may be noted that these characteristics of energy balance are probably related to the fact that the over-all body protein content of goldthioglucose-obese mice is increased over the normal; we have seen above that this is not true in obese-hyperglycemic mice, in spite of their enlarged liver, heart, kidney and gastro-intestinal tract. Thus, even the characteristics of the way in which obese-hyperglycemic mice achieve their positive energy balance are different from what is seen in a purely regulatory syndrome. Obese mice show not only a different food pattern and an abnormal energy balance, they have food choices which are different from those of non-obese littermates. While these, placed on a free choice situation, will normally consume a high carbohydrate diet, obese-hyperglycemic mice will select a high fat diet[29]. The inactivity and the placidity of obese-hyperglycemic mice is another behavioral abnormality which distinguishes them from normal or from non-obese littermates made obese by goldthioglucose[33].

As the name of the syndrome indicates, obese-hyperglycemic mice have high blood glucose levels, on the average. These develop at about the 12th week. All animals do not necessarily show this characteristic[27]. There is a minority of obese mice whose blood sugars are in the high ranges of normal. Maximum blood sugars recorded in untreated animals are of the order of 600 mg. per cent. That the syndrome shows unity, however, in spite of this variability in absolute values of blood sugar levels, is shown by the fact that all other characteristics of the syndrome are present and that even in obese animals, in which the blood sugar is in the high normal range, hyperglycemia can be readily elicited, for example, by the administration of growth hormone[34, 35]. The blood glucose levels are sensitive to fasting, will drop to the high normal fasted range when such animals are deprived of food for any length of time. Blood glucose levels are not lowered by carbutamide and tolbu-

tamide; they are lowered by saccharin[36] (and as will be seen below by diethyldithiocarbamide[27]). Growth hormone administration produces a drastic increase in blood sugar[34, 35, 37]. For example, in one group there was an increase of 204 mg. per cent 12 hours after treatment. If the animals are properly selected, this increase in blood glucose levels following growth hormone administration is reproducible often enough so that it can be used as a method of assaying this hormone. The glucose tolerance of obese-hyperglycemic mice after growth hormone treatment is markedly impaired. Fasting abolishes the growth hormone response, and carbohydrate-free regimens significantly lower the response. By contrast, non-obese or goldthioglucose-obese animals show a very transient response of their blood sugar to growth hormone. Such a response may be noticeable three hours after injection but has completely disappeared 12 hours after growth hormone administration, by which time obese-hyperglycemic mice show their peak response.

Cortisone also increases blood glucose in obese-hyperglycemic mice, while ACTH does not have any appreciable effects[37]. By contrast, cortisone, as well as corticotropin, has no effect in goldthioglucose-obese and in non-obese animals. Obese mice are not killed by 20 units of insulin, even when given such doses repeatedly under fasting conditions. Non-obese control animals treated under similar conditions (or goldthioglucose-obese mice) are always killed by such doses of insulin. The fed obese-hyper-glycemic mice display hyperglycemic responses to glucagon or epinephrine[38]. A 12-hour fast does not abolish this response. By contrast, the hyperglycemic response of non-obese mice to epinephrine and glucagon is definitely decreased by a fast of this duration. The levels of liver glycogen per gram of liver are similar in obese-hyperglycemic and non-obese controls, but because of the much larger liver mass, the obese mice have more than twice as much total glycogen[39]. This, incidentally, is a nonspecific effect of hyperphagia and obesity: mice made obese by goldthioglucose also show a much larger liver and more liver glycogen. Levels of glycogen in representative skeletal muscles are also higher in obese-hyperglycemic and non-obese controls. The turnover of liver glycogen as measured by incorporation of uniformly labeled C^{14} is approximately six times as great for total glycogen and three times as great per gram of liver and per mg. of glycogen as their obese-hyperglycemic controls[39]. The hereditarily obese-hyperglycemic mice are extremely sensitive to cold and die of exposure in a few hours[40, 41]. This is in con-

trast to the marked resistance of non-obese mice and of non-obese littermates made obese by goldthioglucose. Pharmacological doses of thyroxin or thyrotropic hormone or dinitrophenol prolong significantly, but not considerably, the life of hereditarily obese-hyperglycemic mice exposed to cold. Corticotropin shortens the duration of survival under the same conditions. Shivering and piloerection do take place in the obese animals. Decreased thickness of pellage cannot be the essential factor, as this is no more marked in these animals than in goldthioglucose-obese mice. Decreased spontaneous exercise can likewise be eliminated by comparing obese and non-obese animals kept in chambers small enough to make movement impossible. Resistance to high environmental temperatures is normal in obese animals. It has been shown that the lack of resistance of hyperglycemic mice recover from exposure to cold as long as their metabolic rate in the cold. Oxygen consumption can readily be doubled in thin animals in the cold under conditions where there is no increase in the obese animals. This failure to increase metabolic rates leads to a drop in body temperature, decreased respiratory rate and Cheyne-Stokes respiration and eventually death. If warmed up again, obese-hyperglycemic mice recover from exposure to cold as long as their central temperature does not drop more than 14 to 16 degrees below their previous normal temperature. High frequency electromagnetic waves can substitute for this missing thermogenesis in genetically obese mice. If these animals are put in the cold but subjected to this type of irradiation they will survive indefinitely[42]. That the lack of resistance in the cold is not due to hypothyroidism is seen from the normal appearance of the thyroid and also from the fact that radioactive iodine uptake by the thyroid is normal in this syndrome. An anoxia test, which has been shown to be an excellent indicator of thyroid function, reveals no abnormality in the obese-hyperglycemic mice[43]. The fact that corticotropin treatment does not improve resistance to cold, the normal or near normal appearance of the adrenals, and the fact that adrenalectomy does not prevent weight gain and prevents high blood sugar only temporarily, argues against an adrenal abnormality[44], as an explanation for the lack of resistance to cold and for the obese-hyperglycemic syndrome generally. From an enzymatic standpoint a number of interesting peculiarities have been observed. There is increased intestinal absorption of glucose[45] and probably correspondingly increased enzymatic activity of the intestinal mucosa, but this is common to all animals which have been

fed large amounts of carbohydrate, particularly in other types of obesity, and appears to be a nonspecific effect of hyperphagia. The skeletal muscle and kidney hexokinase activities are of the same order as that seen in non-obese animals or in goldthioglucose-obese animals[46]. Similarly, there appears to be no increase in liver glucose-6-phosphatase activity. (This is in contrast to the situation in mice made obese by grafting ACTH-secreting tumors[47]; this situation is also in contrast with the situation seen in alloxan diabetes, in which there are decreased hexokinase and increased glucose-6-phosphorylase activities.) By contrast, the liver phosphorylase activity per unit weight of liver in the obese-hyperglycemic mice is significantly greater than in the non-obese controls[46]. This finding is, of course, in keeping with the accelerated liver glycogen turnover previously described and with the postulated etiology. The blood cholesterol is elevated in obese-hyperglycemic mice[48, 49]. The serum cholesterol levels in animals four or five months old is doubled and tends to increase further as the animals get older. A number of dietary and hormonal treatments further increase cholesterol levels in these animals, in particular high protein diets, fasting and growth hormone. High serum cholesterols are also seen in ACTH-obese mice and in yellow female obese mice, but not in goldthioglucose or stereotaxic hypothalamic-obese mice, at least to anywhere near the same extent. Blood lipids are increased, with the animals showing the blood protein pattern generally seen in obese animals[50]. The characteristics of lipogenesis in these animals are remarkable and have been used to characterize metabolic obesities as opposed to regulatory obesities. In all forms of obesities where the animals are allowed to overeat there is increased lipogenesis as the animals become obese. In animals where hyperphagia is solely a result of error in regulation of food intake, lipogenesis goes back to normal when the animals are pair-fed with controls or are compared to controls in the fasted state. By contrast, where a metabolic abnormality is at the root of the syndrome and in turn causes the hyperphagia, the situation is quite different[8, 9, 16]. In such cases, lipogenesis from C^{14}-acetate is still increased even when hyperphagia is eliminated by pair-feeding or by comparing the animals in the fasted state[25, 35, 51-53]. This is true *in vivo* —the same phenomenon persists when lipogenesis from C^{14}-acetate is studied in liver slices[54]. That this phenomenon is not simply a matter of isotope dilution has been demonstrated by showing that the acetate pool was not smaller in the obese-hyperglycemic mice than in the controls.

In fact, when acetate dilution was taken into consideration, results became even more striking[55]. A further analysis of this phenomenon has been undertaken by examining the metabolism of epidydimal and mesenteric adipose tissue from hereditary obese-hyperglycemic mice and comparing these tissues to those of normal goldthioglucose-obese and ACTH-secreting tumor-obese mice. Glucose-1-C^{14}, -6-C^{14}, Pyruvate 1, 2, or 3-C^{14} and acetate 1 or 2-C^{14} were the substrates used in the absence or presence of added insulin or added growth hormone. Glucose uptake, oxidation of C^{14}, incorporation of C^{14} into fatty acids, the alpha and beta carbon of cholesterol, and into glycogen were carried out. In goldthioglucose-obese mice, glucose uptake and C^{14} incorporation is reduced to the same extent. Lipogenesis and shunt activity are even lower in elderly animals. (Age is not a factor in lipogenesis and controls.) While pyruvate and acetate metabolism are normal in goldthioglucose mice, pyruvate metabolism is somewhat reduced in obese-hyperglycemic mice, and this impairment increases with age. As regards acetate metabolism, there is normal oxidation of C^{14} in obese-hyperglycemic mice but considerably increased incorporation into fatty acids[56, 57]. These metabolic characteristics also explain why it has been found that while the rate of mobilisation of fatty acids is normal in obese-hyperglycemic mice, unlike what takes place in goldthioglucose animals, there is a tremendous resynthesis of the mobilised fatty acids. If carboxyl-labeled palmitate is fed to the two types of obese animals, it is found that the label stays in the carboxyl group in the goldthioglucose animals, so that the decrease in radioactivity is a fair measure of the rate of oxidation of the fat. By contrast, it is found that the label is rapidly spread all along the carbon chain in obese-hyperglycemic mice. This indicates that breakdown to two carbon fragments does take place, but that resynthesis occurs, so that the decrease in radioactivity, while it gives a picture of the oxidation of fatty acid *carbon*, does not give a picture of the turnover of the fatty acid *molecules*[58]. The fact that fat synthesis still takes place in fasted animals or in animals placed in the cold (even when also fasted) explains the lack of resistance of these animals to cold. Instead of being able to oxidize the fatty acids they mobilize, part of the molecule is resynthesized and thus is not available for thermogenesis[59]. These metabolic characteristics may also explain why, when obese hyperglycemic mice are fasted, they retain a high proportion of their fat, so that even when brought back to control weight they still contain an amount of fat very

much in excess of normal, a characteristic shared with other forms of metabolic obesities which also show an increased lipogenesis under fasted conditions[60, 61].

Finally, these metabolic characteristics may also explain why, in metabolic obesities in general and in the obese-hyperglycemic syndrome in particular, fasting causes no increase (in fact causes a drop) in blood ketones[62]. This is in contrast to the situation in regulatory forms of obesity, where the increase in blood ketones under fasting conditions takes place as in normal animals. The primary error in the pathogenesis of this syndrome appears to be the hyperglycemia with hyperinsulinism. It has been shown that the pancreatic insulin content is very much increased, as is circulating insulin activity[63, 64]. Increased availability of insulin together with increased circulating glucose would, of course, increase lipogenesis and hence obesity. What, in turn, the hyperglycemia is due to is less firmly established. It has been hypothesized that this was due to increased pancreatic glucagon secretion by the alpha cells. In support of this view is the fact that increased pancreatic glucagon is seen after growth hormone treatment (which further increases the hyperglycemia)[65]. Also, treatment with diethyldithiocarbamate, which damages the alpha cells, eliminates the hyperglycemia and the response to growth hormone[27].

Obese-hyperglycemic mice have a somewhat shorter life expectancy than normal animals. When repeatedly reduced and allowed to eat *ad libitum* again, their life expectancy is further reduced[66]. One frequent cause of death seems to be evolution of the hyperglycemia toward true diabetes. Infections are not infrequent. On the other hand, the obese-hyperglycemic mice are more resistant than their controls to ascites tumors[67].(Goldthioglucose-obese mice are more prone than their controls to mammary tumors: when dealing with the relationship of obesity to tumors, one should define what tumor and what obesity[68].)

Other forms of genetic obesity have been less intensively studied in the mouse, though they also establish metabolic characteristics of some of the types. Yellow mice are a type of genetic obesity which has been known for over 50 years. The first good description of yellow obese mice was given by Cuénot in 1905. Since then, a number of studies dealing with genetics, reproduction, and growth of these animals have appeared[69,70,71]. The syndrome is a dominant heterozygous form of genetic obesity, with the homozygous combination lethal. Castle ob-

served that yellow mice are slightly longer than non-obese littermates[72], a finding confirmed in our laboratory[68]. While some authors have observed that in their colonies the females were heavier than the males, this was not so in our experience. Our yellow males were heavier than females throughout the growth period, the difference being at least as great as that between control males and females. Yellow mice exhibit some sensitivity to cold in that while they do survive in the cold they do not become obese. Weight gain is greatest on high fat diets. As yellow mice are given an opportunity to exercise in activity cages, they lose weight. Fasted blood glucose levels are normal while fed blood glucose levels are frequently elevated in males. Yellow male and female mice show a degree of insulin resistance. Yellow males show a marked hyperglycemic response to growth hormone, ACTH, cortisone and glucagon. Females exhibit hypercholesteremia[68]. As in other forms of metabolic obesity, blood ketones are decreased by an 18 hour fast[62]. The mechanism of the obesity is unknown. Bielschowsky and Bielschowsky[73] have described another form of hereditary obesity which they have called the New Zealand strain. The animals do mate (unlike obese-hyperglycemic mice), and nurse their young. The blood glucose is markedly elevated. Stilbestrol corrects some of the metabolic abnormalities—it lowers the elevated blood sugar and prevents or reduces excessive deposition of fat. Insulin is tolerated in doses fatal to normal mice. The authors express the opinion that these animals show hyperinsulinism and that "a pituitary factor, not yet identified, opposes the action of insulin".

One form of regulatory obesity, hypothalamic obesity, has been known to occur spontaneously at a fairly high frequency in a stock studied by Vidal and de Robertis[74]. It is possible that the stock contains a hereditary predisposition to spontaneous degeneration of the ventromedial nucleus of the hypothalamus. Genetic obesity has also been observed in rats in association with diabetes[75] and in the Shetland sheep dog, where it was transmitted along recessive patterns[76]; and of course in a number of strains of domestic animals, the large white hog in particular.

* * *

The demonstration of the hereditary nature of familial obesity in Man is much more difficult. That obesity does "run in families" is well established. In a series of over 1,000 obese patients in Vienna, Bauer[77] found that 73 per cent had one or both parents obese. This figure is

close to that of 69 per cent found by Rony[78] for a series of 250 patients in Chicago. In his studies in Philadelphia, Angel[79] found that half of the offspring of obese × average parents were obese, as were two-thirds of the offspring of obese × obese matings. Eighty per cent of the obese children had at least one fat parent; the parents of 25 per cent were both obese. Gurney[80] in a previous survey of a similar population had found that only 9 per cent of the children of average-weight parents were overweight. Fellows[81], studying the overweight fraction of a life insurance sample, found that 58 per cent of the mothers and 43 per cent of the fathers of these individuals were or had been overweight. Dunlop[82], studying a group of obese subjects in Edinburgh, found that 69 per cent had at least one overweight parent (39 per cent, mothers only; 12 per cent, fathers only; in 18 per cent both parents were overweight).

Ellis and Tallerman[83], studying 50 very obese children, found that 60 per cent of them had a parent or a sibling similarly affected; in particular, 26 per cent had a grossly overweight mother, 12 per cent a grossly overweight father, 6 per cent both parents grossly overweight. Iversen[84], following 40 obese children, found that in 88 per cent (31 cases) one or both parents were obese. Only in 10 per cent (4 cases) was there no obesity in parents or siblings. Our own studies in Boston suburbs[11] also show a high degree of correlation between overweight in parents and in children.

Interpretation of these data is difficult, as cultural background interacts with genetics to determine the incidence of overweight. Angel[79] found that the large obese group which he studied showed a relative excess of first and second generation Americans; 42.7 per cent had American-born parents (more than half "old Americans"); 8.7 per cent were American-born with one foreign-born parent and one American-born parent; an unusual 35 per cent were American-born of foreign-born parents and 13.6 per cent were foreign-born. On the other hand, while it has been claimed on the basis of small samples that children of South European[79] and Jewish[83] stock have an unusually high incidence of obesity, studies in Boston did not confirm this. Fry[85] did not find any significant association between ethnic (white) origin and severity of obesity. Johnson and co-workers[11] did not find any significant difference between the incidence of obesity in two well-to-do suburbs of Boston: Brookline (mostly Jewish) and Newton (mixed background). The fact that in the southern United States overweight is more pre-

valent in white males than in white females but less prevalent in Negro males than in Negro females[86] may be the result of a socio-economic situation wherein Negro men are still frequently employed in jobs entailing physical labor while Negro women no longer are, but are not yet subjected to social pressure for weight control. On the other hand, this difference between the white and the Negro population may be determined, at least in part, by genetic factors.

The possible interaction of environmental and genetic factors, the mixed genetic background of most human groups—particularly in Europe and North America—the fact that human genetics deals with generations whose life expectancy is similar to that of the geneticists, and that some of the most useful tools of genetics (e.g., parent-offspring, brother-sister mating) are not applicable to human studies, emphasizes the significance of two tools which *are* applicable to problems such as that of genetic factors in human obesity; i.e., the study of twins and the study of sex ratios.

Evidence much more cogent of the importance of genetic factors in the etiology of at least some forms of obesity other than the simple demonstrations of the frequent familial association is derived from Siemens' *Zwillings-Pathologie*, the study of diseases in twins[87]. The method is, briefly, as follows: assuming that it is possible to diagnose with accuracy identical (monozygotic) and fraternal twins, it is then reasonable to say that pathological and other characteristics which, if they occur at all, are always or nearly always present in both members of identical twin pairs, but rarely or never appear in both members of fraternal twin pairs, are hereditary. (This statement does not imply the reverse, i.e., that characteristics which are found in members of both types of pairs are not hereditary.) The "twin method" has been applied by Newman, Freeman and Holzinger[88] to measurable characteristics such as height, weight and intelligence quotient. In this case, comparison of the variability of the quantity measured in identical twins and in fraternal twins permits a preliminary assessment of the role of heredity and that of environmental factors. (A comparison of variability among siblings and individuals of the same age and sex leads to obviously far less clear-cut distinction between environmental and hereditary causation.)

The study of Newman and associates bore on a large number of subjects, identical and fraternal twins and siblings of like sex. Variability

of weight was included among the many physical and mental characteristics compared[88]. The correlation between identical twins for weight was found to be extremely high (0.973), exceeded only (and barely) by that for standing height (0.981), higher than right and left finger ridges (0.919 and 0.931) and intelligence characteristics (Binet, 0.910, Woodward-Methews, 0.562). The ratio of standard errors of estimate of weight for fraternal twins to identical twins is 2.2 (22.96 lb. for fraternal twin weights as compared to 10.33 lb. for identical twin weights), of the same order as height or head length and superior to all such ratios for mental traits. When twins and siblings are paired (the siblings being taken at comparable age), the mean pair difference in weight of siblings is 10.4 lb. (with 32.5 per cent differing by more than 12 lb.), that of fraternal twins is 10.0 lb. (with 34.5 per cent differing by more than 12 lb.), and that of identical twins is 4.1 lb., with only 2 per cent differing by more than 12 lb.

Von Verschuer[89], studying 57 pairs of identical twins, aged 3 to 51 years, found weight somewhat more variable than other physical characteristics, but still very constant from twin to twin. Average percentage variation amounted to only 2.58 per cent. A separate calculation for those identical twins reared and living in identical environments and for those reared and living in dissimilar environments showed the average percentage variation in body weight for the first group to be 1.39 per cent and for the second group 3.6 per cent. These results would tend to demonstrate that, while environmental factors play a role in the control of body weight genetic factors are of paramount importance.

Suggestive of the importance of genetic factors in the etiology of human obesity is the finding[79, 80] that segregation can be shown to take place in the transmission of obesity. If the various types of matings, stout × stout, stout × non-stout and non-stout × non-stout are considered, the variability of weight of the offspring is relatively small for the first type (most [73 per cent in his study] offspring stout), least for the third type (almost none [9 per cent in his study] of the offspring stout), and largest for the stout by non-stout matings (offspring almost evenly divided between obese [41 per cent] and non-obese [59 per cent]). This is interpreted by Gurney as showing that stout individuals carry gametes for slenderness while slender individuals rarely carry gametes for stoutness.

Finally, perhaps the most striking indication of genetic determina-

tion in human obesity is the demonstration by Angel[79] that the sex ratios of children in the various types of matings (as characterised by weight) are statistically different from that for the population as a whole. There are fewer males (and larger families) among the progeny of average × average matings and fat male × average female matings than among the offspring of fat × fat and average female × fat male unions. This is not inconsistent with an hypothesis that one of the genes which in some cases helped to determine obesity is a sex-linked recessive lethal gene. Such sex-linked recessive lethals do very probably occur in man. Such a gene might be expected to be more frequent among the females of the average × average matings with at least one obese daughter, where presumably the interactive non-recessive genes mainly responsible for obesity would be less frequent than in matings involving one or more fat parent (especially a fat father). On the other hand, the relatively larger family size of the average × average and fat female × average matings may have purely psychological or social-biological and not genetic determinants. Likewise, the relative excess of fat females over fat males among the parents and siblings of the obese (about 60 per cent of females are fat as opposed to 40 per cent of males) may express as strongly the effects of genetic sex limitation and social sex differences in activity as the effects of a hypothetical sex-linked recessive lethal factor which present data are inadequate to test. Here Angel[79] notes that we are hampered by inability to record the potentially obese as well as the actually obese phenotypes.

CONCLUSION

It is my hope that the evidence presented in this lecture has illustrated a number of points. First, that genetic factors do influence body weight and may cause obesity. Second, that obesity is the common end-product of a great many conditions which may have very little in common except the occurrence of a positive energy balance. Third, that if these conditions differ in mechanism, their treatment ought to differ—for example, if inactivity is an essential aspect of a particular syndrome, increased activity may be more effective than caloric restriction alone. From the point of view of public health, it would appear more profitable to recognize the role of genetic factors and use them to anticipate obesity than to deny obvious facts. The use of genetics has

been highly successful in terms of detection and early prevention as regards diabetes. Once it is recognized that the children of obese subjects are much more likely to become obese, preventive efforts could be similarly concentrated on such vulnerable individuals. Proper food and exercise habits could be taught early. All workers in the field are in agreement that the longer obesity has lasted, the more malignant it is apt to be. Recognition of genetic factors may thus help to prevent obesity from ever appearing or at least from developing in many individuals. Once again, our treatment of obesity is likely to be more successful if we view this condition as a medical, rather than a moral problem.

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ORAL HISTORY: LIVING MOMENTS OF MODERN MEDICINE*

SAUL BENISON, PH.D.

LORD Balfour recounts that when Robert L. Stevenson was a boy, he turned to his mother while at play one day and said, "Look, Ma, I have drawed a man; now I am going to draw his soul". I can say unequivocally that Oral History is not an attempt to draw men's souls. We leave the problem of the human soul to the theologians who over the centuries have tenaciously tried to establish claims to that elusive property; or to writers who exalt, damn and constantly try to define its qualities; or to the artists who timelessly have tried to represent it by line and color. This is not to say, however, that historians have not wrestled with the soul. Mr. Toynbee's massive volumes, to name but one historian of note, are impressive testimony that from time to time historians also engage in this kind of exercise.

The oral historian's function is much more modest: we collect the autobiographies of contemporaries for use of future historians. We are engaged, if you will, in establishing an archive of autobiographical materials. In a sense we help create a particular kind of personal document because we implicitly believe that the details of an individual human life will serve to illuminate and help differentiate for the future historian those vast forces which in our own time, ironically enough, assault the identity of the individual.

Learning about the individual has particular relevance for the history of science. Speaking to such a point some years ago, the distinguished historian of science, George Sarton, advised:

> "The history of science and in particular the history of medicine is not simply an account of discoveries. Its purpose is to explain the development of the scientific spirit, the history of man's reaction to truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice. Discoveries are evanescent for they are soon replaced by better ones. The historian must try not only to describe these evanescent discoveries but to find in science that which is timeless. When he

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> does that he comes very close to the historian of art. To put it in other words a man's name may be immortalized by his discoveries. Perhaps there was nothing else in him deserving of remembrance? He may have been a poor sort of man, a man whose mind was as sharp and narrow as a knife's edge? Or else the historian betrayed him. In so far as a scientist is also an artist his personality can survive, otherwise not. It is the historian's main duty to revive the personalities, rather than to enumerate their scientific discoveries. Discoveries may be important but personalities are infinitely more so. . . ."

For Sarton, as for other humanists, the individual is at the core of history. But just what his role is or how far he shapes his history is not precisely known. It is, moreover, a subject of tense debate—a problem that has gnawed at historians from Thucydides to the present day. Tolstoy defined it in *War and Peace* in the following manner:

> "As in the question of astronomy then, so in the question of history now, the whole difference of opinion is based on the recognition or non-recognition of something absolute, serving as the measure of visible phenomena. In astronomy it was the immovability of the earth, in history it is the independence of personality—free will."

The problem of the role of the individual in history is one that constantly besets the historian gathering the memoirs of his contemporaries. There are others.

In our own age historians are faced with an anomaly. The technology of the printing press, paper and chemical industry, typewriters, etc., has given us the means of producing documents which historians are agreed is almost the first thing that is necessary if one is to write history. Langlois, the great French medievalist, put it in the aphorism "Pas de documents, pas d'histoire". Anyone who has visited the National Archives or the Library of Congress in Washington knows that in these two institutions alone there are enough documents bearing on the history of the United States to keep several generations of historians profitably at work. I need not speak of other repositories. But the very technology that has helped to create these documents has also helped to eliminate the personal document of letter, diary or autobiography. The tempo of living has increased to such a degree that few today sit down leisurely at the end of a day to write in a journal, much as Emerson or John Q. Adams did, or to write long personal letters to family and friends. Why write when the telephone is at hand and five minutes of talk produces as many words as a two hour, 15 page letter? An hour's plane ride and a face to face meeting do away with a week of correspondence between two scientists in Boston and New York. The dis-

appearance of the personal document is of particular importance to the person interested in the history of medicine and in particular the history of the medical revolution that has occurred in this country in the last 50 years, for at the center of that revolution stands the physician or medical specialist—in part participant, in part product of that change. Although there is a vast amount of data available about that revolution, there is a notable lack of personal documents—and the human detail, the atmosphere of the day-to-day life of the physician is missing. For example, Dr. Joseph Aub of the Massachusetts General Hospital, now hard at work collecting documents for a joint biography of David Edsall and Walter Cannon, finds that it is almost impossible to find any Edsall papers. If anyone in this room attempted to write a history of the development of physiology in this country he would find an important gap in his material for the last half century because the papers of two notable pioneers, Graham Lusk and Eugene DuBois, have disappeared.

The Oral History project in medicine was designed to fill this gap by capturing on tape the recollections of distinguished physicians, surgeons, teachers of medicine, and medical scientists. This excursion into autobiography not only gives us a self-portrait of the contemporary physician, how he views his profession, disease, health and rehabilitation; it also gives us rich insights into such diverse topics as the development of diagnosis, surgical technique, instruments, process of research, medical education and hospital life.

How do we gather these autobiographies? For the historian who conducts the interview, the work is arduous. He must prepare as if he, in fact, were going to write a biography of the individual interviewed. He must not only read all available primary material that is extant (papers, letters, etc.), he must also become acquainted with the history of the institutions his subject has been associated with (schools, hospitals, societies, laboratories, cities) as well as his specific medical interest (surgery, bacteriology, physiology). This latter chore is most important because only by doing this can he learn to trace the development of the medical problems that his subject has been concerned with. He cannot, in fact, overlook the commonplaces of everyday life that both interviewer and subject take for granted. So if a subject says, "by using the classic techniques available I separated . . .", it is best to stop him and ask him to detail those techniques, for what is classic today might not be classic 50 years from now. Actually, there is always a third party

present at each interview: this is the historian yet unborn who continually interrupts *sotto voce* and asks, "Are you getting everything I will need to know?" It is not an easy burden to realize that in the future you may be regarded a fool who missed a golden opportunity. Unlike the sociologists, we have no set of formal questions, not that such questions have no value—they do. Our problem is not that of quantitating data. In essence we are data gatherers. As a matter of fact, in addition to gathering recollections, much effort is expended in collecting any extant papers, diaries and photographs.

I have often been asked, "How do you know you are getting the truth?" The answer is simple: I don't know. At best, memory is tenuous and even well-intentioned people often misremember. Sometimes they lie or, to use a less harsh word, fib; sometimes their prejudices rewrite events in such a manner as to make a professional propagandist blush. All of this all men do. First, it is well to remember that none of these autobiographies is presented to the historian of the future with the notation that it is the final and most accurate word. In the end it will be received as but one of many documents. The future historian will in fact use it, weigh it, examine it in relation to other extant documents. His evaluation of it will be keener because time will furnish him still more evidence and new perspective.

What about the fellow who lies or creates a myth? It should be pointed out that the physician who creates a myth is also unwittingly giving us a portrait of himself, and that the collection of untruths and prejudices is as valuable as collecting what passes for pristine truth. Sometimes it is the contradictions that emerge from the various memoirs that pose the nicest historical problems. While interviewing physicians in New York, all were agreed that a change in the treatment of typhoid fever (feeding patients a high caloric diet) occurred after Coleman and DuBois' notable experiments on the basal metabolism of typhoid patients in 1911. When I spoke with Dr. Aub in Boston I learned another story. He maintained that Dr. Fred Shattuck fed his patients a high caloric diet long before the work of DuBois and Coleman. Who was right? In the strictest sense all were telling the truth as they saw and understood it. As a matter of record, a check of the hospital records at the Massachusetts General Hospital reveals that Dr. Shattuck did feed his typhoid patients a high caloric diet at least 10 years before DuBois and Coleman's experiments at Bellevue. The real problem, however, is

not who was first; it is, what forces led to a change in the treatment of typhoid fever in the first decade of the 20th century? Once this question is posed the beautiful diversity that exists in history becomes apparent. Different factors played a role in Boston and New York. Vital statistics show that there was a marked decline in the number of typhoid cases in Boston beginning in 1890, due in large measure to the rigorous inspection of the water and milk supplies of that city. This decline was also manifest in the number of typhoid patients who were admitted to the M.G.H. It was this decline which allowed Shattuck, a superb clinician trained in the French school of pathology (strongly rooted in Boston medicine from the days of James Jackson, Bigelow and O. W. Holmes), to arrive empirically at the observation that if he fed his patients a rich diet, they survived; if he starved them (as was the traditional practice), they died. Although such great figures as Hermann Biggs played an important role in New York public health matters, as late as 1909 there were terrible epidemics of typhoid in New York due to contaminated milk supply. It was not, for example, until 1910 that the New York Board of Health adopted a requirement providing that all milk used for drinking purposes be properly pasteurized. DuBois' training was markedly different from that of Shattuck. Educated at the College of Physicians and Surgeons of Columbia University, DuBois, under the urging of the distinguished pediatrician John Howland, turned his interests to physiological problems, and took postgraduate training in physiology in Krause's clinic in Berlin. It was here that he learned the intricacies of physiological research, including the use of the Pettenkofer-Voit chamber used in the studies of basal metabolism. It was in Germany, for example, that DuBois met, for the first time, the distinguished pioneer in nutrition research, Graham Lusk, who later became his associate at the Russell Sage Institute of Pathology at Bellevue. It was under Lusk's urging that both DuBois and Coleman applied their researches on basal metabolism to the study of disease and, in particular, typhoid fever. Yet before those researches could come to fruition, there was almost an insurmountable obstacle to be overcome. It was necessary to measure the body surface of both normal and abnormal individuals. The mathematical formula to measure the body surface did not come from Coleman or DuBois; it came from DuBois' cousin, Delafield DuBois, an electrical engineer who was theoretically concerned with a similar problem in

his own work. The diversity here described gives rise to a whole new series of problems. For example: Why weren't Shattuck's views adopted? Were they widely disseminated? What was the state of communication within the medical profession in 1900? In a sense the problem bears a close resemblance to the problem of the discovery and use of ether. There is little doubt that Dr. Crawford W. Long, a graduate of the University of Pennsylvania, discovered the anesthetic properties of ether long before Wells or Jackson. Again, the point is not who was first but rather who helped integrate it into acceptable medical practice.

I should like to turn now and discuss the project itself. To date the following physicians and medical scientists have cooperated with the project: the late Alan Gregg of the Rockefeller Foundation; A. R. Dochez, Professor Emeritus of Medicine at P. and S.; the late Eugene F. DuBois of the Cornell University Medical College; David P. Barr, Professor Emeritus of Medicine at Cornell; Connie M. Guion, Professor Emeritus of Medicine at Cornell; Edward D. Churchill, John Homans Professor of Surgery at Harvard; I. S. Ravdin, John Rhea Barton Professor of Surgery at the University of Pennsylvania; Dana W. Atchley, Professor of Clinical Medicine at P. and S.; René Dubos, Member and Professor at the Rockefeller Institute; Joseph C. Aub, Professor Emeritus of Medicine at Harvard; and the late Abraham Flexner of the General Education Board of the Rockefeller Foundation.

I have been asked on occasion, how do you know these people are really important? Again I must answer, I don't really know, but I think that it would be well for us to remember here the wisdom of Henry Sigerist. In his justly famous introduction to *A History of Medicine*, he wrote:

> "History remembers many names and has forgotten many. A strange process of selection takes place. Doctors who were very popular during their life-time, who had their portraits painted by famous masters and had large size engravings made from them, may be completely forgotten today, and when we have to catalogue such a portrait we may have great difficulty in finding out who the man was. Others remained or became famous after their death. They all had to appear before the tribunal of history. Historians with the advantage of being able to look at events from a distance examined, interpreted and evaluated their lives and work. . . . Every society has an ideal physician in mind whose characteristics are determined primarily by the social and economic structure of that society and the technical means available to medicine at that time. Interpretations and evaluations change: that is why there is no such thing as a definitive history."

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*Knudsen, E. T., and Rolinson, G. N.: Lancet 2:1105 (Dec. 19) 1959.

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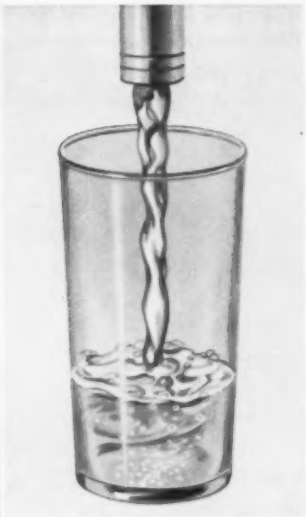

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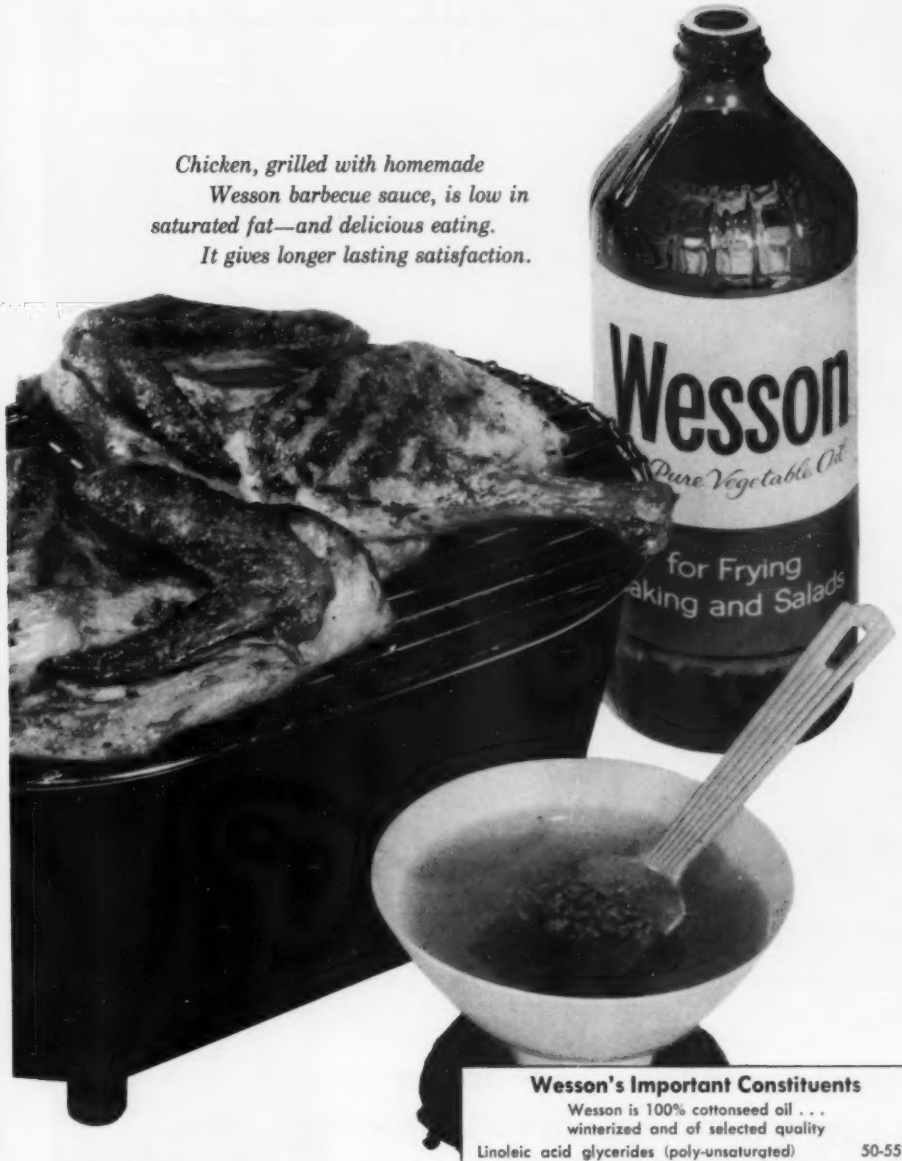

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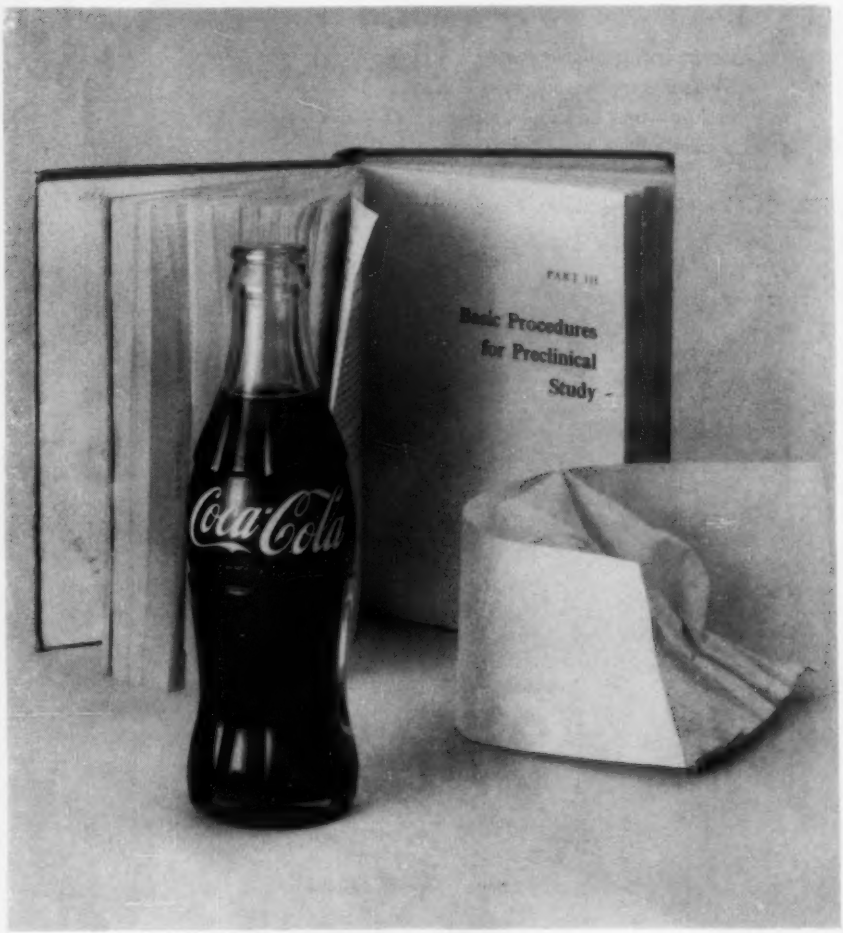

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Ref: Plotz, M.: Modern Management of Obesity, J.A.M.A. 170: 1513-1515 (July 25) 1959.
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Blumenthal, L.S., and Fuchs, M.: Am. Pract. & Digest Treat. 9:1121 (July) 1958.

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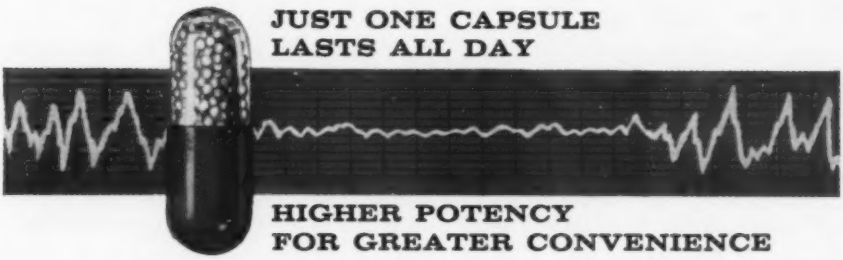

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Lysaught, J. N., and Cleaver, W.: Paper presented at the Symposium on Antibacterial Therapy, Michigan and Wayne County Academies of General Practice, Detroit, Sept. 12, 1959 (published Nov., 1959)

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references. (1) Antos, R. J.: Southwestern Med. *40*:695-697 (Nov.) 1959. (2) Tullis, I. F.: Initial Experience with a Simple Weight Control Formula, to be published. (3) Roberts, H. J.: Effective Long-Term Weight-Reduction—A Therapeutic Breakthrough, to be published.

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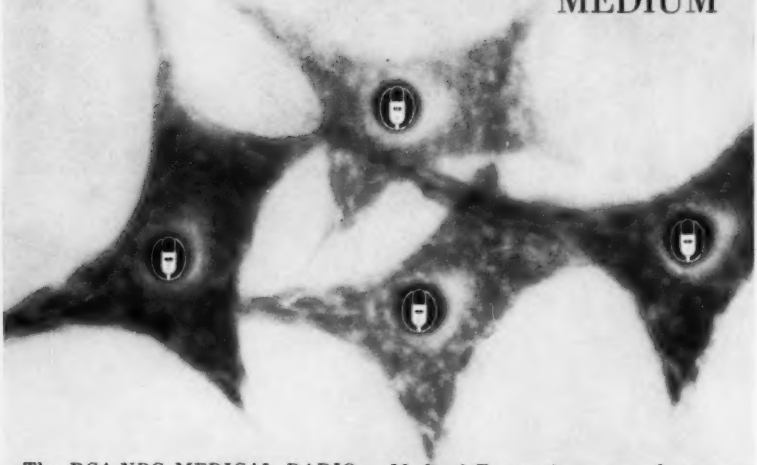

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